

RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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JUNE 1959

No. 6

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RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES
PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

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Pantopaque Myeloencephalography¹

ROBERT MONES, M.D., and ROBERT WERMAN, M.D.*

THIS IS A report of a new neuroradiologic procedure for the demonstration of abnormalities of the posterior fossa and upper cervical region. By the technic described below, we are able to fill the third and fourth ventricles, cisterna magna, and posterior rim of the foramen magnum with Pantopaque instilled by way of a *lumbar puncture*. For convenience we call this procedure myeloencephalography.

Positive contrast examination of the ventricles has been useful for many years, earlier with Lipiodol and more recently with Pantopaque. In all the studies reported in the past twenty years a direct ventricle approach through a burr-hole had been used for achieving internal filling. We are not aware of any systematic study of the posterior foramen magnum and cisterna magna with a positive contrast substance.

METHOD

Nine to twelve cubic centimeters of Pantopaque are injected into the lumbar subarachnoid space, as for routine myelography. The spinal needle is removed and the patient is placed on his back, in the horizontal position, and then, under fluoroscopic control, is tilted cephalad 45 to 55°. The fourth ventricle, cisterna magna, and posterior aspect of the third ventricle can be recognized quickly and usually fill

within a few minutes. Anteroposterior and lateral films are then taken and the patient is brought to a horizontal position, where another series of anteroposterior and lateral exposures is made.

The procedure is simple and entails much less maneuvering than routine cervical myelography. Originally fluoroscopy was not employed, and the patients were usually tilted 70 to 85° downward (1). Recently we have found fluoroscopy a great aid. In patients with posterior fossa masses one must sometimes allow for slow filling of the ventricles.

The anteroposterior and lateral views, obtained with the patient in the horizontal position, are occasionally of aid in patients in whom the third ventricle shows filling but the fourth ventricle does not. Pantopaque in the third ventricle will run into the posterior part of the fourth ventricle when the patient is moved from the tilted position to the horizontal plane. The posterior rim of the foramen magnum is also usually better defined in the series of pictures taken in the horizontal plane than in those in the tilted position.

If the films are satisfactory, the patient is placed with the head in the erect position for five minutes. Pantopaque leaves the ventricles and cisterns, pools in the lumbar region, and is then removed. A few drops may remain in the ambiens or pontine cis-

¹ From the Department of Neurology, The Mount Sinai Hospital, New York, N. Y. Accepted for publication in October 1958.

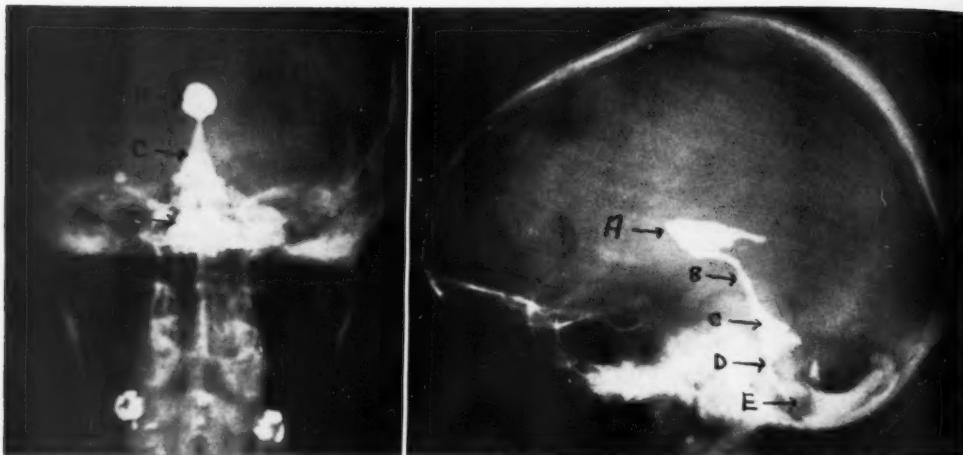


Fig. 1. Case of 40-year-old man with suspected posterior fossa disease. The myeloencephalogram was normal and shows the excellent definition possible with this technic. Pantopaque is seen in the third ventricle (A), aqueduct of Sylvius (B), fourth ventricle (C), foramen of Magendie (D), and cisterna magna (E).

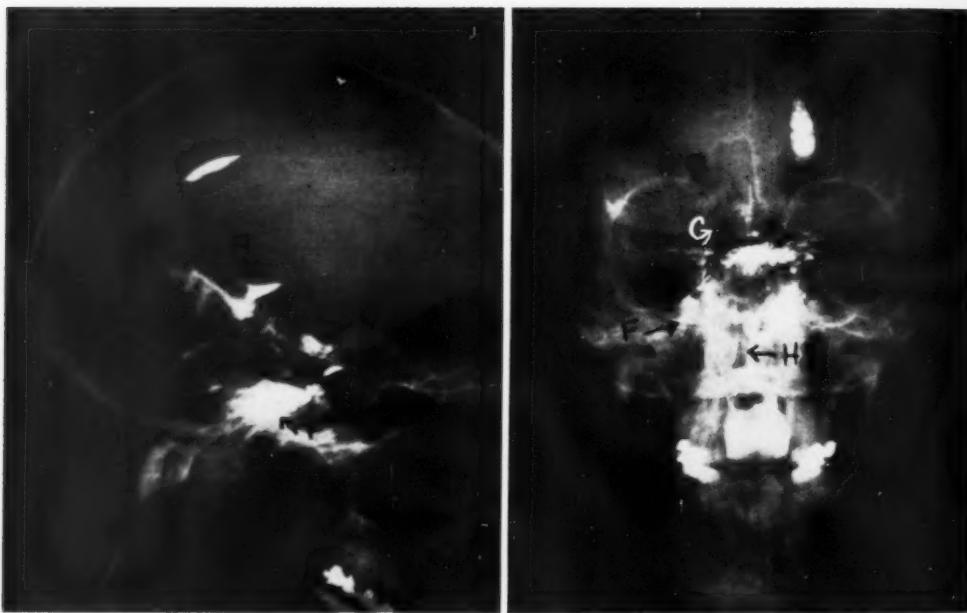


Fig. 2. Case of 21-year-old female with evidence of brain stem and cervical cord disease. The absence of filling of the cisterna magna is abnormal. Pantopaque may be seen in (F) the cerebellar-pontine recess, (G) interpeduncular cistern, and (A) posterior portion of the third ventricle. The basilar artery is outlined (H).

At postmortem examination the patient was found to have malformations of the upper cervical vertebrae, basiocciput, and the brain stem. Platysmia was present.

terns. The entire procedure takes approximately twenty minutes (Fig. 1).

There are many cases in which the pathologic anatomy is uncertain and the diagnosis rests between a high cervical, a foramen

magnus, and a posterior fossa lesion. In these cases we first do routine cervical myelography with the patient in the prone position. After the cervical cord, the anterior aspect of the foramen magnum,

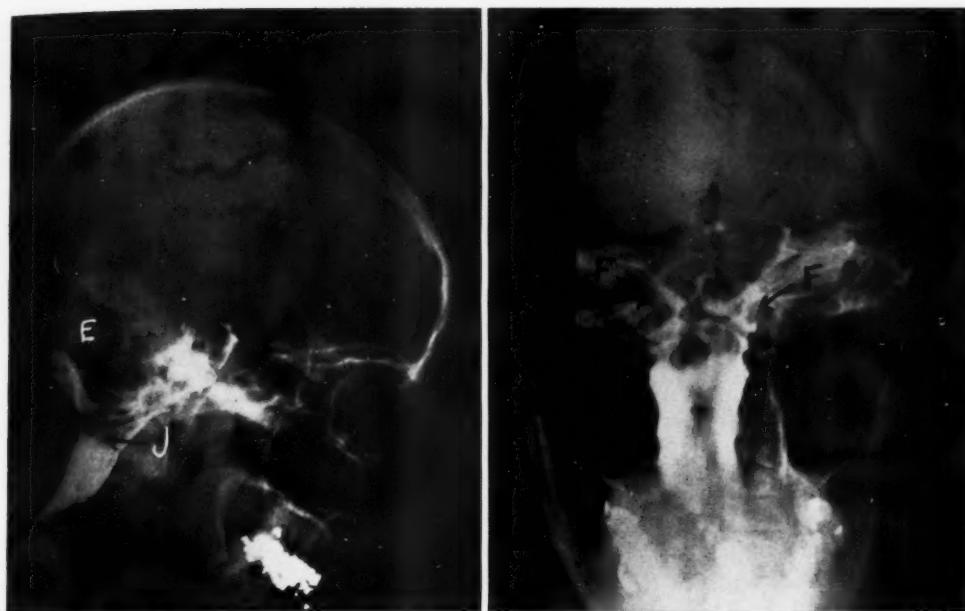


Fig. 3. Case of 45-year-old woman with proved hemangioma of the right cerebellum. Pantopaque study shows the inferior border of the cerebellum (J) to be well below the foramen magnum. The cisterna magna (E) is smaller than that usually seen. There is almost no filling of the cerebellar-pontine recess which is usually in area F. The pneumoencephalogram in this case did not show ventricular filling. The abnormalities of the tonsilar region and the various cisterns of the posterior fossa were not definitely shown by air study.

and the pontine cisterns have been studied, the patient is turned on his back and the examination is completed as described above. We feel that both the posterior and anterior aspect of the foramen magnum should be investigated if there is a suspicion of trouble in this area.

RESULTS

Myeloencephalography was performed in 40 patients (Table I), and in every instance we were able to define the posterior rim of the foramen magnum. In 2 cases the cisterna magna showed no filling. Both of these patients had proved abnormalities of the posterior fossa. One had verified platybasia and bony malformations of the cervical vertebrae (Fig. 2). The other had a medulloblastoma of the cerebellum.

In 31 cases the inferior margins of the cerebellar tonsils were definitely identified. In 5 cases, the tonsil border, as shown by the Pantopaque study, was well below the level of the foramen magnum. Four of the 5 patients had verified tumors of the cere-

TABLE I: EXPERIENCE WITH MYELOENCEPHALOGRAPHY IN FORTY CASES	
A. Filling of fourth ventricle obtained.....	23 cases
Brain stem diseases	
Tumors.....	8 cases
Others.....	7 cases
Cervical cord-foramen magnum disease	
Etiology unknown.....	8 cases
B. Nonfilling of fourth ventricle.....	17 cases
Brain stem diseases	
Tumors.....	11 cases
Vascular lesions.....	3 cases
Platybasia.....	1 case
Aquaduct stenosis.....	1 case
Supratentorial tumor.....	1 case

bellum (Fig. 3); 1 had a tumor of the posterior corpus callosum, unverified by operation.

Ventricular filling generally corresponds to the success or failure of ventricular filling in pneumoencephalography. In the 40 cases examined, the fourth ventricle was filled in 23. Among the 17 cases without ventricular filling were 11 associated with posterior fossa masses; 10 of these did not show ventricular filling on pneumoencephalography. There was 1 case of unverified syringomyelia in which the fourth ven-

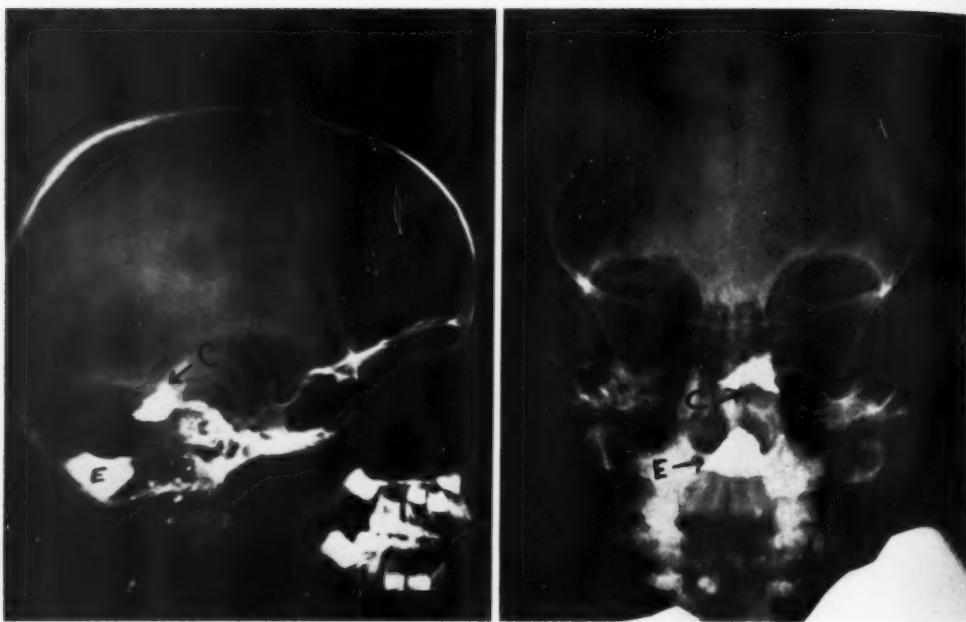


Fig. 4. Case of 9-year-old child with signs and symptoms of an upper brain stem lesion on the right side. Surgical exploration showed no obvious tumor of the cerebellum and it was assumed the patient had an anteriorly placed lesion.

The previous pneumoencephalogram showed poor definition of the fourth ventricle. The Pantopaque myeloencephalogram demonstrates a definite shift of the fourth ventricle (C) from right to left. The cisterna magna (E) is quite large.

TABLE II: IMPORTANT INFORMATION AFFORDED BY
MYELOENCEPHALOGRAPHY NOT DEMONSTRATED BY
PNEUMOENCEPHALOGRAPHY

Shift of fourth ventricle.....	3 cases
Normal fourth ventricle.....	1 case
Obstruction of aqueduct.....	1 case
Herniated cerebellar tonsils.....	5 cases
No filling of cisterna magna.....	2 cases

tricle filled whereas filling had not been achieved on pneumoencephalography. In 6 cases myeloencephalography was unsuccessful in filling the fourth ventricle though part of the ventricular system had been filled on pneumoencephalography. In these cases, however, the fourth ventricles were not invariably well defined by air. Some of the failures and instances of nonfilling of the ventricles occurred early in the series before optimal techniques were established. The 10 patients in whom combined cervical myelography and myeloencephalography were done because of suspected posterior fossa, foramen magnum, or cervical cord disease, showed good filling of the cervical subarachnoid space,

fourth ventricle, and various cisterns. No abnormality was found in these cases.

When posterior fossa lesions are suspected, pneumoencephalography is done. If ventricular filling is obtained, it may still be equivocal, as the fourth ventricle is not always well outlined. In 4 instances the superior definition of the fourth ventricle with Pantopaque, compared to air (Fig. 4), was of importance in managing the case (see Table II). In 1 case the Pantopaque failed to flow past the fourth ventricle, giving evidence of an aqueduct block (Fig. 5). In 7 patients abnormalities of the cisterna magna or tonsillar position as shown by Pantopaque were of help in confirming the presence of an intracranial abnormality. Six of the 7 had proved tumors and the other a congenital malformation.

DISCUSSION

In 1923, Sicard in France described in detail x-ray studies of the spinal cord

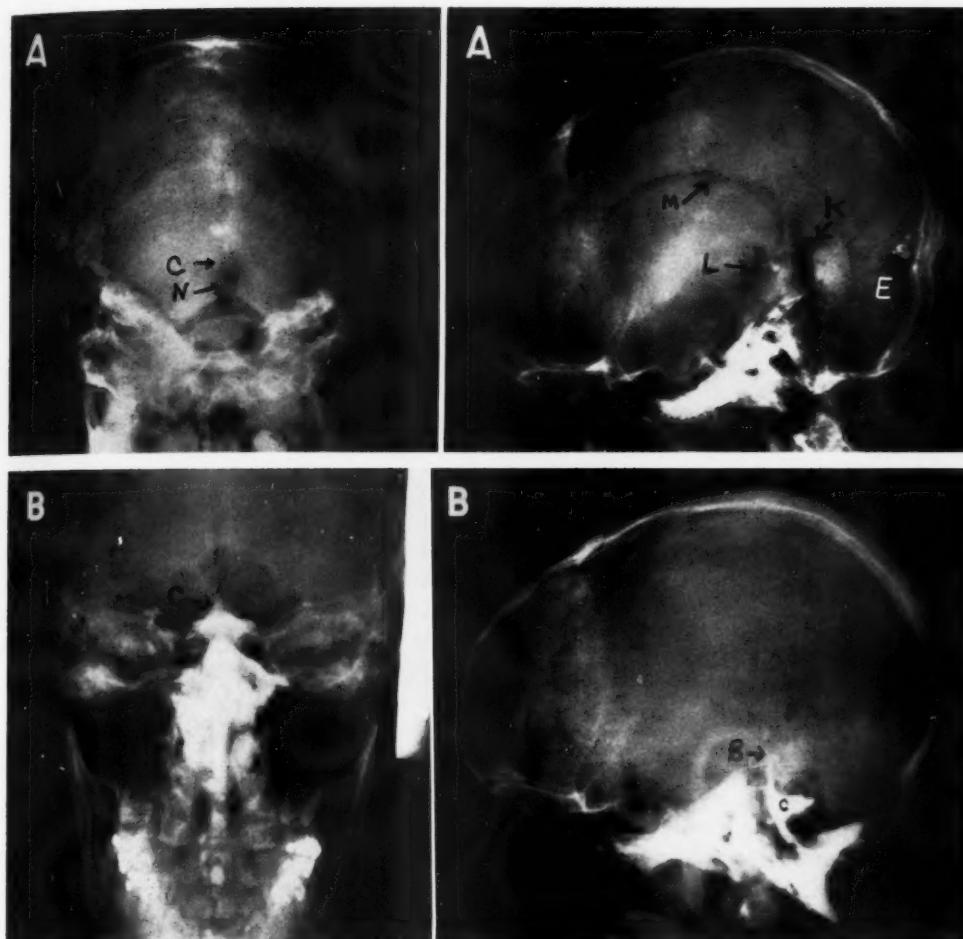


Fig. 5. Case of a 17-year-old patient complaining of headache. Examination showed bilateral papilledema. AA. The pneumoencephalogram showed filling of the cisterna magna (E), cisterna venae magnae cerebri (K), cisterna ambiens (L), cisterna corporis callosi (M). The fourth ventricle cannot be seen in the lateral view. In the anteroposterior view the shadow labeled C may represent partial filling of the fourth ventricle superimposed on the vallecula air shadow (N).

BB. The Pantopaque myelogram shows excellent definition of the fourth ventricle (C). The Pantopaque did not flow past the cephalad portion of the fourth ventricle, giving evidence of an aqueduct block (B). The fourth ventricle has an abnormal configuration in the lateral view. The anteroposterior projection shows the structure to be in the midline (C).

After the above studies, burr-hole ventriculography was done with air and Pantopaque by the neurosurgical staff. This study showed excellent filling of the third ventricle with Pantopaque. The surgeons were unable to fill the aqueduct or fourth ventricle *via* the third ventricle.

A Torkildsen procedure was done with good results (six-month follow-up).

with light and heavy Lipiodol. He noted casually that occasionally Lipiodol (the form that was lighter than water) would rise into the ventricles, giving excellent definition of their anatomy, but this observation was not followed up. In 1930, Balado (2), an Argentine neurosurgeon,

reported 90 cases of ventricular study in which Lipiodol was instilled by burr-hole and ventricular puncture. For the past ten years Pantopaque has been widely used by neurosurgeons for positive contrast ventriculograms. Articles by Bull (3) and Horwitz (4) have emphasized the low

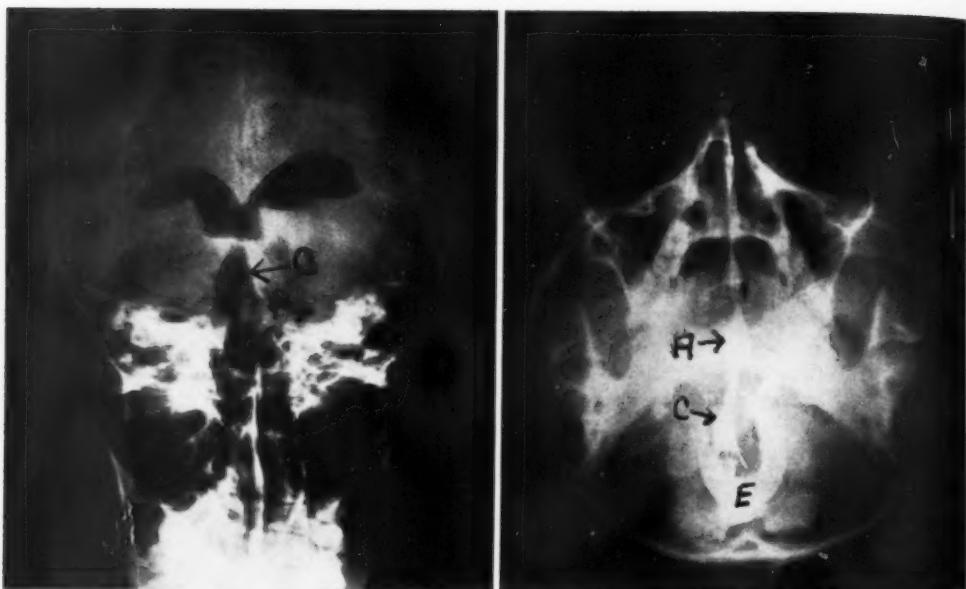


Fig. 6. Case of a 27-year-old man with signs and symptoms of a mass in the left cerebellar pontine angle. This was verified by surgical exploration and removal.

The pneumoencephalogram (left) shows the fourth ventricle (C) shifted from left to right. Erosion of the petrous bone is noted (P).

Myeloencephalography was done in the routine manner, as described. An extra view taken in a base projection (right) shows the posterior fossa structures in detail. A. Third ventricle. C. Fourth ventricle shifted from left to right. E. Cisterna magna.

incidence of morbidity with this medium and the excellent studies of the third and fourth ventricles.

Pneumoencephalography is an excellent procedure for demonstrating posterior fossa abnormalities. When posterior fossa lesions are suspected (with or without papilledema), pneumoencephalograms should be obtained. Using standard technics, we usually fill the third and fourth ventricles and the cisterns of the region. Frequently, however, there is difficulty in interpretation of the films because of confusing air shadows from cisterns which are superimposed on the ventricles. This is particularly true of the postero-anterior projection, in which outlines of the cisterna magna, third ventricles, fourth ventricles, vallecula, and interpeduncular cisterna may be superimposed. It is sometimes difficult to see the fourth ventricle on lateral views because of large mastoid air cells. Pantopaque provides superior definition of the fourth ventricle in equivocal cases. It also

affords excellent definition of the posterior foramen magnum region, the cisterna magna, and the border of the inferior margin of the cerebellar tonsils. Important information can be gained from Pantopaque myeloencephalography that is not always possible by pneumoencephalography.

The procedure as described above is simple and is associated with only mild discomfort. The patient usually complains of headache or a sense of fullness in the head after being tilted downward for three to five minutes. The discomfort is less than that during pneumoencephalography and the procedure, in this respect, is comparable to myelography. The neurosurgical use of Pantopaque instilled directly into the ventricles has not been complicated with morbidity (3, 4). Pantopaque arachnoiditis in myelography has been reported (5, 6, 7), but the cases (if valid) are few considering the number of myelograms done with this medium.

One patient of the 40 described in this paper had a reaction characterized by fever, pleocytosis and meningeal signs. The entire episode disappeared after a week, with no complications in a five-month follow-up. We have rarely observed similar reactions with routine myelography. No other reactions or sequelae were seen.

CONCLUSION

Myeloencephalography is a new method of studying the structures of the posterior fossa. With use of this procedure burr-hole ventriculography can frequently be avoided for positive contrast studies of the third and fourth ventricles. Myeloencephalography is also useful in diagnosing abnormalities of the posterior foramen magnum, such as herniated cerebellar tonsils, bony abnormalities, Arnold-Chiari malformations, and tumors.

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SUMMARIO IN INTERLINGUA

Myeloencephalographia a Pantopaque

Es describite un nove technica pro le demonstration de anormalitates del fossa posterior e del region supero-cervical. Le autores lo designa como myeloencephalographia. Inter novem e dece-duo centimetros cubic de Pantopaque es injicite in le lumbar spatio subarachnoide e röentgenopelliculas es obtenite con le paciente in position inclinate, con controlo fluoroscopic, pro permitter replenation del quarte ventriculo, del cisterne magne, e del aspecto posterior del tertie ventriculo, e de novo post le retorno del paciente al position horizontal.

Iste technica esseva usate in 40 pa-

tientes, con relativemente leve grados de disconforto. Un sol reaction de severitate significative occurreva, e isto dispareva intra un septimana, sin ulle complication observate in le curso de cinque menses.

Myeloencephalographia a Pantopaque se provava utile in le diagnose de anormalitates del foramine magne posterior, per exemplo herniation del tonsillas cerebellar, anormalitates ossee, malformation de Arnold-Chiari, e tumores. In certe casos, informationes importante que non es accessibile al pneumoencephalographia esseva obtenite gratias al technica de myeloencephalographia.



Positive Contrast Ventriculography¹

McCLURE WILSON, M.D., and S. R. SNODGRASS, M.D.

IN THE COURSE of a neuroradiologic investigation of the brain, it is sometimes imperative to obtain unequivocal radiographic visualization of the third ventricle, the aqueduct of Sylvius, and the fourth ventricle. This can usually be done with gas as the contrast substance. Occasionally, however, gas will not enter the regions it is desired to visualize, or a small, gas-filled cavity cannot be clearly separated from the shadows of superimposed structures. This last difficulty can sometimes be resolved by laminagraphy. There will remain, however, a small number of cases in which even this modality, when available, will fail.

It is possible to fill the small midline ventricular cavities with a contrast material of very high density, such as Pantopaque. When this is done, the ventricular outlines can be seen, clearly and distinctly, on radiographs. This technic has been called "positive contrast ventriculography." While it has been known for almost thirty years (1), it has never attained widespread use in this country, so far as we can determine from a review of the literature. Readers who are interested in the historical background are referred to the papers by Bull (2) and Horwitz (3).

Those who have written on positive contrast ventriculography describe different methods of conducting the procedure (2-4). It is preferably done under local anesthesia, in order to secure the patient's active co-operation, though general anesthesia may be satisfactory. In our experience, the decision to undertake positive contrast ventriculography is usually made at the time of gas ventriculography. Therefore, in most of our patients the procedure was done under general anesthesia. It is of interest to note that when positive contrast ventriculography has been done inde-

pendently of gas ventriculography, the discomfort and febrile reaction have been minimal.

METHOD

Except in infants, it is necessary to have a surgical burr hole in the skull. This is usually already present, due to the fact that gas ventriculography will have been done previously. The patient is seated upright in front of a vertical fluoroscope, and is positioned so that the fluoroscopist can obtain a good lateral view of the skull. The neck and body are flexed, until the foramen magnum lies at a higher level than the vertex. The head is then rotated 45°, so that the side containing the burr hole is uppermost.

A needle is introduced through the burr hole into the lateral ventricle, and 1 to 2 c.c. of Pantopaque is injected, the amount depending upon the estimated size of the third ventricle as seen on previous air studies, if such are available. If the head has been properly positioned, the Pantopaque will run along the superior and medial wall of the lateral ventricle and will come to rest in the anterior horn. The patient's head is then rotated back to the sagittal plane and his body is straightened up, but his head and neck are still held in flexion.

Under fluoroscopic control, the neck is gradually extended. The Pantopaque will be seen to flow along the floor of the anterior horn, dripping through the interventricular foramen into the third ventricle. When all of the Pantopaque is in the third ventricle, films are made in the antero-posterior and lateral projections, without change in position of the head. The films will show the anterior portion and floor of the third ventricle.

Without moving the patient's head, the x-ray tube and film are positioned for

¹ From the Department of Radiology (M. W.) and the Department of Surgery, Division of Neurosurgery (S. R. S.), University of Texas Medical Branch, Galveston, Texas. Accepted for publication in November 1958.

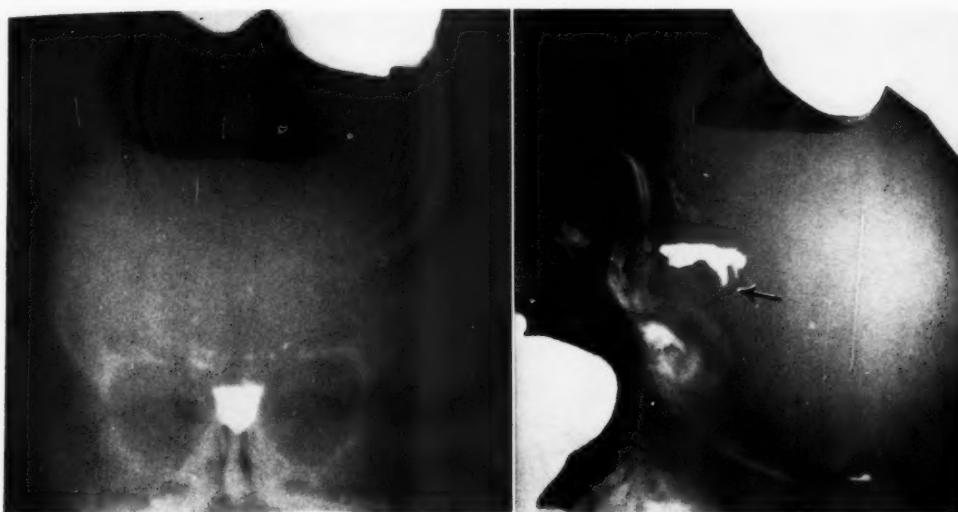


Fig. 1. Case I. The lateral and third ventricles are dilated and there is an obstruction of the aqueduct of Sylvius. The aqueduct is not displaced. Autopsy revealed aqueduct stenosis.

another lateral film. When all is ready, the neck is hyperextended as much as possible. Three seconds are allowed to elapse, and the exposure is made. This film usually produces good visualization of the posterior portion of the third ventricle and the aqueduct of Sylvius. The patient is immediately placed in the supine position, with neck and head extended, and antero-posterior and lateral films are again obtained. These films usually show the fourth ventricle to best advantage.

The neck is then flexed and the head of the table is raised. If no obstruction is present, the Pantopaque will flow out of the fourth ventricle and down the spinal canal, to collect in the dural sac at the base of the spine. Here it may be removed by spinal puncture, although this step has usually been omitted in our patients.

An alternate method consists in injection of the Pantopaque with the patient prone on a tilt table. After injection, the head of the table is gradually raised and the progress of the Pantopaque along the floor of the anterior horn and into the third ventricle is checked by repeated lateral views of the skull. When the opaque material is all in the third ventricle, the patient is quickly turned over on his back with his

head and neck extended. This maneuver will trap the Pantopaque in the posterior part of the third ventricle, the aqueduct, and the fourth ventricle. Films can then be obtained. This method is best for large, heavy patients under a general anesthetic.

Recently, a method was described whereby the fourth ventricle was filled from below, by Pantopaque injected into the subarachnoid space in the lumbar spine (4).² We have had no experience with this procedure.

If there is an obstruction which prevents the Pantopaque from leaving the ventricular system, it cannot be removed. This raises the question of possible adverse effects upon the ependyma. Bull (2) states that a postmortem examination was performed in 4 of his cases and no evidence of ependymitis was found. He describes the patients as "moribund" when the procedure was done but does not state the interval of time between positive contrast ventriculography and death. In 4 of our patients autopsies were performed. In each instance the interval between the ventriculographic study and death was very short, the longest being forty-seven days. No changes attrib-

² See also preceding paper.



Fig. 2. Case II. In the lateral view, the fourth ventricle was not displaced, but in the anteroposterior projection it was shown to be pushed far to the right. There was no obstruction. Surgery revealed a hemangioblastoma of the left cerebellar hemisphere.

utable to the Pantopaque were found in the brains of these patients. Various studies have been done on the effects of Pantopaque which has been left in the subarachnoid space of the spinal canal for long periods of time (5-8). From these reports, it appears likely that Pantopaque can cause arachnoiditis. So far as we can determine, no studies have been conducted regarding the late effects of Pantopaque on the ependyma in man, although some animal studies are available (9). It is our belief that, in selected cases, the advantages of positive contrast ventriculography as a diagnostic tool outweigh the possible disadvantage of late adverse effects on the ependyma.

During the year 1957, 243 air-contrast studies of the brain were performed in our institution. Positive contrast ventriculography was done in 11 (4.5 per cent) of this number. The following cases illustrate the usefulness of the procedure.

CASE REPORTS

CASE I: L. G., a one-month-old white girl, was admitted to the hospital because of gradual enlargement of the head. Delivery had been normal. When the child was first seen, the head measured 41 cm. in circumference.

Ventriculography showed internal hydrocephalus, with absence of the septum pellucidum. The third

ventricle and aqueduct were not visualized. A positive contrast ventriculogram (Fig. 1) disclosed dilatation of the third ventricle and an occlusion of the sylvian aqueduct 1 cm. caudal to its origin. The diagnosis of aqueduct stenosis was made. The child died a few hours after ventriculocisternostomy was done. A postmortem examination confirmed the diagnosis of aqueduct stenosis.

CASE II: R. S., a 15-year-old white male, had for several months experienced intermittent attacks of vertigo and vomiting, associated with headache. These attacks gradually increased in frequency and were almost constant at the time of admission.

When examined, the patient held his head tilted and turned to the left side. Co-ordination of the left extremities was poor. The Romberg test was strongly positive.

Pneumoventriculography showed that the lateral and third ventricles were normal. The fourth ventricle as seen in the lateral films appeared normal. It could not be clearly identified in the postero-anterior projection. A positive contrast ventriculogram (Fig. 2) showed marked displacement of the fourth ventricle to the right in the anteroposterior view but no displacement in the lateral projection.

Operation revealed a hemangioblastoma in the left cerebellar hemisphere.

CASE III: K. M., a 14-year-old white female, three days prior to admission became ill with headache and diplopia and rapidly lapsed into a coma. When seen at the hospital, she was lethargic and disoriented. She had a left central facial paralysis. The eyegrounds were normal.

On vertebral arteriography the basilar artery was seen to be of rather small caliber and its branches would not fill. A ventriculogram revealed normal

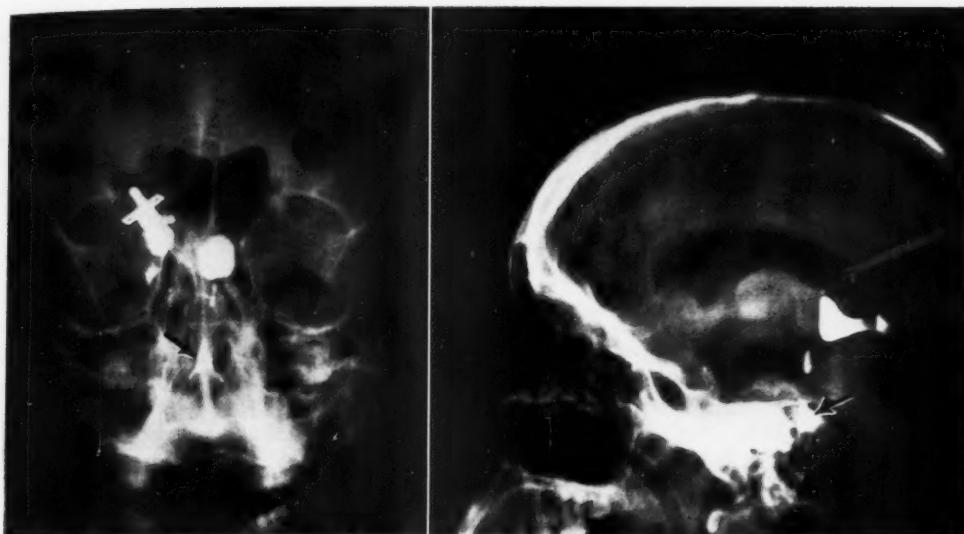


Fig. 3. Case III. The fourth ventricle and aqueduct were in normal position in the anteroposterior and lateral projections. A large superior pineal recess is filled. Autopsy revealed thrombosis of the right superior cerebellar artery.



Fig. 4. Case IV. The posterior portion of the third ventricle and the aqueduct are displaced forward. The fourth ventricle appears to be displaced slightly downward. Diagnosis of tumor of the mesencephalon was not verified.

lateral and third ventricles. The aqueduct and fourth ventricle could not be clearly seen. A positive contrast ventriculogram (Fig. 3) showed the aqueduct and fourth ventricle to be in normal position and not dilated. Therefore, surgery was not performed. The patient died two days later.

Postmortem examination showed a thrombosis of the right superior cerebellar artery.

CASE IV: G. M., a 40-year-old white male, had experienced severe intermittent occipital headaches for three years. Although there were long intervals between the headaches at first, they gradually became more frequent and had been of daily occurrence for six months prior to admission.

Neurologic examination showed nothing definitely abnormal. Roentgenograms of the skull revealed

a faint area of calcification in the region of the pineal gland. Air studies, including ventriculogram and pneumoencephalogram, were done. The posterior portion of the third ventricle and the aqueduct were not clearly identified and a positive contrast study was undertaken (Fig. 4). This showed forward displacement of the aqueduct of Sylvius. A diagnosis of a tumor in the region of the mesencephalon was made. A ventriculocisternostomy was performed, followed by x-ray therapy, and the patient was discharged to the care of the referring physician. At follow-up eight months later, he was asymptomatic.

DISCUSSION

In a considerable experience, we have found positive contrast ventriculography of great value in certain instances. We have encountered no false positive findings, and complications have been infrequent. High fever for a day or two has, at times, followed the procedure. This has occurred almost exclusively in infants in whom massive dilatation of the ventricular system existed and in whom pneumoventriculography had been performed earlier on the same day. The frequency of high temperatures following pneumoventriculography in such patients is well known to clinicians. In 2 such infants a diagnosis of meningitis was subsequently made following culture of Gram-negative organisms from the ventricular fluid; both of these patients recovered. If meningitis actually occurred in these patients, it is impossible to attribute it definitely to one or the other of the two procedures done. In a large experience with Pantopaque myelography, we have not encountered meningitis or other infectious complications; we would not expect the introduction of Pantopaque into the ventricular system to be followed by infection more frequently than myelography.

Positive contrast ventriculography has been of great value in the study of infants with noncommunicating hydrocephalus. The limited quantity of gas which may be introduced into the greatly dilated ventricular system without seriously disturbing the general condition of these patients often fails to demonstrate adequately the third ventricle, aqueduct, and

fourth ventricle. By the use of this method, stenosis of the sylvian aqueduct has been demonstrated by us with a frequency and certainty not possible with methods previously used.

It is our feeling that positive contrast ventriculography, while helpful in patients with tumor of the cerebellum, is not frequently required in the study of that group. Usually, gas ventriculography will adequately demonstrate these lesions. We have, however, had good success with positive contrast ventriculography in such lesions when the diagnosis was otherwise uncertain.

SUMMARY

A method for visualizing the third ventricle, aqueduct of Sylvius, and the fourth ventricle with Pantopaque is described. The procedure has proved of definite value in some cases of lesions around the third ventricle and in the cerebellum. Its greatest value is in demonstrating lesions in the region of the midbrain and pons. As this region is not susceptible to direct surgical attack, pathological confirmation of the diagnosis was not available in several of our patients. Unequivocal localization of neoplasms involving the pons or mesencephalon has helped us to avoid unnecessary negative operations and has established the need for other therapeutic measures. Positive contrast ventriculography has been used only when gas studies failed to provide the necessary information.

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SUMMARIO IN INTERLINGUA

Ventriculographia a Contrasto Positive

Per replenar le micre cavitates ventricular del linea central con un substantia de contrasto de alte densitate, per exemplo con Pantopaque, il esseva trovate possibile demonstrar le contornos de illos clar- e distinctemente. Le technica esseva designate como "ventriculographia a contrasto positive."

Le substantia de contrasto es introducite via un foramine burinato. Le technica es describite, e plure casos de su application es reportate pro illustrar le utilitate de illo. Illo se ha provate de valor definite in certe casos de lesions in le vicinitate del tertie ventriculo e in le cerebello. Su plus grande utilitate jace in su empleo in le demonstration de lesions in le region del mesencephalo e del ponte. Le localisation de neoplasmas afficiente iste structuras

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ha essite de adjuta in evitare operaciones innecessari e ha establete le necessitate de altere mesuras therapeutic. Ventriculographia a contrasto positive ha essite de grande valor in le studio de infantes con hydrocephalo non-communicante. Per medio de iste methodo, stenosis del aqueducto sylvian ha essite demonstrate con un frequentia e un grado de certitude que non pote esser attingite con altere methodos.

In lor experientia le autores ha incontrate nulle caso de false positivitate. Complications causate per le manovra ha essite paucu frequente.

Ventriculographia a contrasto positive ha essite usate solmente in casos in que studios a gas non produceva le information requirite.



An Evaluation of the Pharmacological Hazards Resulting from Use of "Viscirodol" in Bronchography

PHILIP M. JOHNSON, M.D., and GEORGE L. IRWIN, M.D.

SINCE ITS introduction in 1956, Visciodol,² a bronchographic agent unique in its high viscosity, has achieved considerable acceptance. Several reports on its use have appeared in the literature (4, 6, 7, 23, 25), all of which have been favorable, the consensus being that it is a superior bronchographic medium. In the largest series of cases (25), 89 per cent of 500 Visciodol bronchograms were judged to be of diagnostic quality, in comparison to 78 per cent of bronchograms performed with Dilonosil Oily. Due to its high viscosity (approximately three times that of Lipiodol), Visciodol enters the pulmonary alveoli infrequently and is eliminated from the lungs with rapidity.

Viscirodol is a suspension of finely powdered sulfanilamide in Lipiodol such that each cubic centimeter contains 320 mg. of sulfanilamide. A preservative, sodium sulfite, is added in trace amounts to prevent oxidation of free iodide. Visciodol is dispensed in 15-c.c. vials, each of which contains 4.8 gm. of sulfanilamide. The sole function of the sulfanilamide is to increase the viscosity of the Lipiodol. A Lipiodol-sulfanilamide suspension has been commercially available abroad for thirteen years, following the discovery by Dormer *et al.* (8) that such a suspension had desirable bronchographic qualities. Visciodol is identical with its European precursor.

The manufacturer's brochure states that "a maximum of 10 c.c. (of Visciodol)... is usually sufficient for one entire lung." This statement does not reflect current practices of most bronchographers. A recent survey (26) of physicians who perform bronchography has shown that the

majority require 30 c.c. or more of contrast material for a bilateral study, whereas only 10 per cent use less than 20 c.c. In their large series, Rayl and Smith (24) used an average of 20 c.c. of Visciodol per lung. In the authors' series, the mean volume required for bilateral bronchography was 29 c.c. This amount exposes the patient to nearly 10 gm. of sulfanilamide.

SULFANILAMIDE ABSORPTION AND METHEMOGLOBIN FORMATION

Interest in the question of Visciodol-induced sulfanilamidemia and methemoglobinemia arose when one of our patients, a 27-year-old man with chronic bronchitis, exhibited generalized cyanosis four hours after bilateral Visciodol bronchography. A blood methemoglobin determination disclosed a level of 26 per cent. Methemoglobinemia cleared in forty-eight hours after multiple administrations of methylene blue. During this period the patient was in no acute distress and exhibited no positive physical findings other than cyanosis. There was no evidence of a sulfanilamide reaction. In this instance an excessive volume of Visciodol had been given inadvertently, but it was considered probable that qualitatively similar phenomena occurred with smaller volumes.

A search of the literature disclosed no investigation of methemoglobinemia following administration of Visciodol or Lipiodol-sulfanilamide for bronchography. Elphinstone (9) stated that he had discontinued use of a Lipiodol-sulfanilamide suspension when the first two patients who received it displayed methemoglobin cyanosis. Burrascano (6) specifically stated

¹ From the Department of Radiology, The School of Medicine, The University of North Carolina, Chapel Hill, North Carolina. P.M.J., Assistant Professor of Radiology; G. L. I., Assistant in Radiology, Fellow of American Cancer Society. Presented at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16-21, 1958.

This investigation was supported by the James Picker Foundation on recommendation of the Committee on Radiology, National Academy of Sciences—National Research Council.

² Marketed by E. Fougera and Co., Inc., Hicksville, N. Y.

that no methemoglobinemia was observed in 40 bronchographic studies with Visciodol, but did not indicate whether his observations were clinical or based upon measurement of methemoglobin levels. Bovornkitti and Zabriskie (4) observed marked cyanosis in 2 children during bilateral bronchography with preheated Visciodol; this cleared following tracheal aspiration, oxygen administration, and postural drainage. Methemoglobin levels were not measured.

Similarly, no reported investigation of sulfanilamide absorption was found in the literature, but it was learned that an unpublished study had been carried out by Jones and Jenkins (18). Dr. Jones has kindly made these observations available (Table III). A group of 9 patients underwent bronchography, during which each received 13 c.c. of Visciodol, containing 4.16 gm. of sulfanilamide. Several days earlier, 5 of these patients had received an oral dose of 4.0 gm. of sulfanilamide. Serial blood sulfanilamide levels were measured in both groups. These data would indicate that in these patients 13 c.c. of Visciodol produced a mild sulfanilamidemia of about twenty-four-hours duration, which was at all times lower than that produced by oral administration of a virtually equal amount of sulfanilamide.

MATERIALS AND METHODS

Patients: Thirty-five patients referred for bronchography and examined with Visciodol constitute the clinical material of this study. The age range was six to seventy-five years, but only one child is included. Twelve of the patients were females. The discharge diagnoses were as follows: bronchiectasis (14 cases), bronchogenic carcinoma (7 cases), pneumonia and tuberculosis (3 cases each), empyema and bronchitis (2 cases each), and lung abscess, bronchogenic cyst, atelectasis, and idiopathic hemoptysis (1 case each). The two criteria for patient selection were that the past history was negative for sulfonamide reaction and that there had been no recent administration of sulfonamides or other methemoglobin-forming drugs.

Bronchography: Twenty-one bilateral and 14 unilateral bronchographies were performed. Each was supervised by a radiologist using fluoroscopic control, while a second physician performed bronchial intubation and Visciodol injection. Pre-medication consisted of a barbiturate drug, parenteral morphine or Demerol, and topical application of Xylocaine 1 per cent. Atropine and other vagolytics were not employed. The majority of patients were examined immediately after bronchoscopy. The Visciodol suspension was thoroughly mixed before administration but was not heated above room temperature. The injection syringe was rinsed in cold water to facilitate expulsion of the medium. The total volume introduced into the bronchi was recorded, with allowance made for residuum in the bronchial catheter. Each patient was instructed to suppress cough, and to refrain from swallowing sputum if cough did occur. On completion of the examination, postural drainage was instituted and cough was encouraged.

Laboratory Technics: Prior to bronchography and at intervals thereafter, blood was drawn for chemical determinations. Sulfanilamide measurements were performed in 34 patients according to the method of Bratton and Marshall (5) in the Biochemistry Laboratory of the North Carolina Memorial Hospital. This spectrophotometric technic measures the number of milligrams of free (active, non-acetylated) sulfanilamide per 100 c.c. of serum. Methemoglobin measurements in 34 patients were carried out in one of the research laboratories of the Department of Pediatrics by an accepted spectrophotometric method (35). Blood for the latter determination was anticoagulated with Sequestrene, hemolyzed, and diluted 1:200 with distilled water. After centrifugation, the supernatant was removed and its optical density (O.D.) found at 510 and 576 $\mu\mu$. The ratio O.D. 576/O.D. 510 was calculated. For each patient a methemoglobin calibration curve was prepared by finding the foregoing ratio for normal blood and for blood in which all hemoglobin

TABLE I: COMPOSITE RECORD OF ALL PATIENTS STUDIED*

Case Age and Sex	Thickness at Discharge	Bronchos- copy	Volume of Viscous (c.c.)	Blood Sulfanilamide Levels in mg. %				Methemoglobin Levels (% of total Hgb.)				Alveolar Spillage (Scale 0-+ + + +)	Vol. Ingested	
				0	2	4	6	24	48	0	2	4		
1. 52 F	Pneumonia	Unilat.	41	0	45.8	47.4	41.5	17.0	11	0	18	9	2	4
2. 47 F	Bronchietasis	Unilat.	40	0	8.0	10.1	8.6	2.6	11	0	0	0	0	++
3. 35 F	Lung abscess	Unilat.	40	0	41.9	36.9	34.0	11.0	11	0	17	10	22	++
4. 23 M	Bronchietasis	Unilat.	37	0	4.6	16.6	20.6	11.2	1.4	0	7	17	21	++
5. 28 M	Bronchietasis	Unilat.	35	0	25.2	21.2	18.9	7.8	1.9	0	0	0	0	++
6. 58 M	Bronchogenic carcinoma	Unilat.	35	0	20.7	27.2	28.2	10.8	1.1	0	2	13	10	0
7. 23 M	Bronchietasis	Unilat.	30	0	14.6	25.0	22.1	5.1	11	0	8	15	8	++
8. 43 F	Bronchietasis	Unilat.	30	0	8.4	10.8	9.1	3.1	11	0	8	15	8	++
9. 14 M	Bronchitis	Unilat.	30	0	2.3	13.8	14.6	4.8	11	0	0	0	0	++
10. 40 M	Pneumonia	Unilat.	30	0	18.6	11.3	11.8	1.1	11	0	0	0	0	0
11. 38 F	Bronchietasis	Unilat.	30	0	16.1	11.3	11.4	4.8	11	0	17	5	1	++
12. 56 M	Bronchogenic carcinoma	Unilat.	30	0	16.0	16.0	16.0	2.4	11	0	6	11	13	0
13. 48 M	Bronchietasis	Unilat.	30	0	23.3	21.3	8.9	2.4	11	0	11	15	13	++
14. 36 M	Bronchietasis	Unilat.	29	0	15.8	17.3	0	0	11	0	8	20	12	++
15. 65 M	Bronchogenic carcinoma	Unilat.	28	0	15.8	10.3	4.2	0	11	0	12	10	10	++
16. 20 M	Bronchietasis	Unilat.	27	0	7.2	10.3	5.9	3.4	11	0	8	10	10	0
17. 20 M	Bronchogenic cyst	Unilat.	27	0	13.7	13.7	10.9	0.8	11	0	10	10	10	++
18. 55 M	Bronchietasis	Unilat.	23	0	13.7	13.7	10.9	5.2	11	0	9	15	9	0
19. 62 F	Tuberculosis	Unilat.	23	0	10.8	10.8	10.8	0	11	0	10	10	10	++
20. 46 F	Bronchietasis	Unilat.	23	0	15.8	15.8	15.8	0	11	0	7	10	10	0
21. 40 F	Pneumonia	Unilat.	22	0	10.8	17.4	18.6	1.2	11	0	9	9	9	++
22. 43 M	Bronchietasis	Unilat.	20	0	8.3	11.2	3.2	0	11	0	6	6	6	++
23. 30 F	Bronchietasis	Unilat.	20	0	10.8	10.8	10.8	0	11	0	10	10	10	++
24. 36 F	Bronchietasis	Unilat.	19	0	1.2	21.6	20.0	0	11	0	7	16	16	0
25. 62 M	Tuberculosis	Unilat.	18	0	3.3	7.2	6.8	4.2	11	0	0	0	0	++
26. 51 M	Empyema	Unilat.	18	0	11.2	9.9	4.2	0	11	0	6	7	0	++
27. 56 M	Atelectasis	Unilat.	15	0	2.0	2.4	2.3	0.8	0.2	0	2	7	7	0
28. 32 F	Hemoptysis of ? etiology	Unilat.	13	0	20.8	16.4	14.6	3.6	0.5	0	11	8	4	++
29. 47 F	Tuberculosis	Unilat.	13	0	1.2	11.2	3.4	0.5	0.5	0	0	0	0	++
30. 51 M	Bronchogenic carcinoma	Unilat.	13	0	1.2	11.2	3.4	0.5	0.5	0	0	0	0	++
31. 52 M	Bronchogenic carcinoma	Unilat.	13	0	1.2	7.3	3.5	0	0	0	5	0	0	+
32. 55 M	Bronchogenic carcinoma	Unilat.	13	0	0	6.0	2.9	0.1	0	0	12	3	3	+
33. 50 M	Bronchogenic carcinoma	Unilat.	12	0	3.7	2.7	2.4	0	0	0	1	0	0	0
34. 75 M	Empyema	Unilat.	10	0	9.8	9.8	8.3	4.4	0	0	2	0	0	0
35. 6 M	Bronchitis	Unilat.	6	0	14.1	18.5	5.0	0	0	0	7	0	3	0

* Excluding all methemoglobin values obtained after administration of methylene blue.

a Case 11: 72 hr. sulfanilamide level = 1.8 mg. %.

b Case 23: 8 hr. sulfanilamide level = 8.7 mg. %.

c Case 28: 1 hr., 8 hr., and 12 hr. sulfanilamide levels respectively = 19.6 mg. %, 12.0 mg. %, 8.0 mg. %.

d Case 31: 12 hr. sulfanilamide level = 4.2 mg. %.

e Case 34: 8 hr. and 12 hr. sulfanilamide levels respectively = 8.0 mg. % and 6.0 mg. %.

TABLE II: RESPONSE OF METHEMOGLOBINEMIA TO METHYLENE BLUE
(Administered in 4th post-bronchogram hour unless specified)

Case	Dose in mg./kg.	Methemoglobin Level, % Before Rx	Methemoglobin Level, % After Rx	Elapsed Time, hr.
12*	1.0	11	4	1.5
16	1.7	12	0	0.5
17(A)†	1.5	8	0	0.5
17(B)*	1.5	7	9	1.5
18	1.5	10	4	0.5
20	2.0	7	3	0.5
22	1.4	6	0	0.5

* Administered at 24 hours.

† Administered at 5 hours.

had been converted to methemoglobin by potassium ferricyanide. These two ratios, representing "zero" and 100 per cent methemoglobin were entered on a graph of which the ordinate indicated per cent methemoglobin and the abscissa the O.D. ratio; these points were then connected by a straight line. From the calibration curve and the O.D. ratio of an unknown sample, the per cent of methemoglobin present, *i.e.*, the per cent of total hemoglobin converted to methemoglobin, could readily be found. Each determination was done within one hour of venipuncture to minimize "decay" of methemoglobin. This method is sufficiently accurate for clinical purposes, although lacking the high refinement of the cyanide conversion method. The range of error is plus or minus 2 or 3 percentage points. Determinations were performed on a Bausch & Lomb "Spectronic 20" spectrometer; randomly selected duplicate samples were spot-checked on a Beckman "B" spectrometer by the same method. No discrepancy was observed in the blood specimens so checked.

Since in this method the methemoglobin level of the blood used for calibration is taken to be zero (before conversion to 100 per cent methemoglobin), the amount of "normal" methemoglobin is automatically disregarded. It has been shown that human blood normally contains up to 2.4 per cent of "inactive" (nonfunctioning) hemoglobin, half of which, or less, is methemoglobin (22). The exclusion of "normal" methemoglobin from the data makes

TABLE III. SUMMARY OF DATA OF JONES AND JENKINS (18): BLOOD SULFANILAMIDE LEVELS (IN MG. PER CENT) AFTER ORAL ADMINISTRATION OF SULFANILAMIDE AND INTRABRONCHIAL ADMINISTRATION OF VISCIODOL

		Hours After Administration				
		0	2	4	6	8
A. Oral administration of 4.0 gm. of sulfanilamide (5 patients)	Mean sulfanilamide level	0	4.6	6.5	6.1	5.8
Patients studied		5	4	5	3	5
B. Intrabronchial administration of 13 c.c. of Visciodol (containing 4.16 gm. of sulfanilamide) (9 patients)	Mean sulfanilamide level	0	2.6	3.8	4.3	3.5
Patients studied		9	6	9	3	9
						1.7

it possible to attribute any methemoglobinemia to the action of absorbed sulfanilamide.

Methylene Blue Effect: In 6 patients the effect of methylene blue was measured by determining methemoglobin levels immediately before and thirty to ninety minutes after intravenous injection of a 1 per cent methylene blue solution. This test was performed four hours after bronchography in 5 cases and at twenty-four hours in 2 cases. The dosage employed was 1.0-2.0 mg./kg. of body weight.

Animal Studies: Four mongrel dogs weighing 13 to 20 kg. were used for comparison of bronchial and gastrointestinal absorption of sulfanilamide from Visciodol. Each animal received an amount of Visciodol equivalent, on a c.c./kg. basis, to the administration of 30 c.c. to a 70 kg. man. It was carefully instilled *via* catheter into the bronchi or into the stomach under fluoroscopic control. Pentobarbital anesthesia was induced for the initial twelve hours of each study to insure that the medium was not dislodged by cough or emesis. Serial blood sulfanilamide determinations were made as described above. Attempts to measure methemoglobinemia were abandoned when it was discovered that in his studies on dogs Wendel (33) had found it impossible of production with sulfanilamide, even in excessively large doses.

RESULTS

Tables I and II contain all data from the clinical investigation. The 35 cases have been arranged numerically according to the volume of Visciadol administered. For comparative purposes the series has been subdivided into three groups on the basis of dosage. Cases 1-7 form *Group I*, in which over 30 c.c. were given (mean: 38 c.c.); Cases 8-26 form *Group II*, in which 16 to 30 c.c. were given (mean: 25 c.c.);

administration of Visciadol, sulfanilamidemia invariably occurred. The magnitude of this sulfanilamidemia is shown in Figure 1. It is seen that the mean concentration of sulfanilamide in the serum exceeded the accepted therapeutic range³ between the second and sixth hours after bronchography. The sulfanilamidemia continued at twenty-four hours and was present in 7 of 8 patients tested at forty-eight hours. In general, as shown by the mean sul-

VISCIODOL BRONCHOGRAPHY: MEAN BLOOD SULFANILAMIDE LEVELS

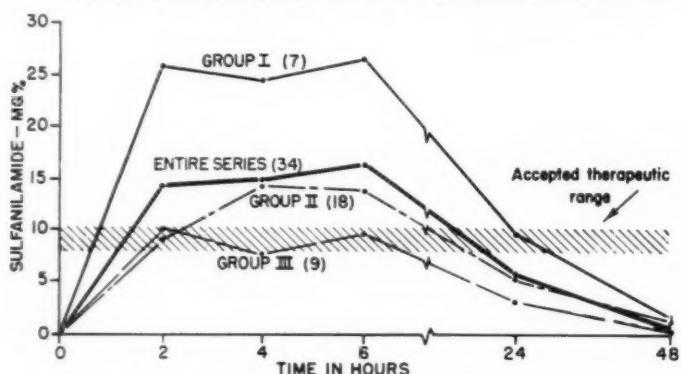


Fig. 1. Graphic demonstration of the magnitude and duration of Visciadol-induced sulfanilamidemia for the entire series and its component groups. The hatched line, indicating the accepted therapeutic blood sulfanilamide levels, is included for comparison.

Cases 27-35 form *Group III*, in which 15 c.c. or less were given (mean: 12 c.c.). Post-bronchography urinary changes were not studied in view of the very high solubility of sulfanilamide in urine. The data in the columns headed "Alveolar Spillage" and "Vol. Ingested" were subjectively derived. These data are the result of an attempt roughly to quantitate these two phenomena, on the basis of (a) the area occupied by alveolar spillage in the post-bronchography postero-anterior chest roentgenogram and (b) an estimate of the proportion of the total administered volume of Visciadol which was swallowed. Internal consistency is claimed for these data, but they are at best semiquantitative.

Sulfanilamide Absorption (Table IV): All patients studied were sulfanilamide-free prior to bronchography. Following

sulfanilamide levels for the three groups, the greater the volume of Visciadol, the greater the resulting sulfanilamidemia.

Figure 2 contains a plot of all sulfanilamide levels for every patient and demonstrates the marked variation of individual peak levels. Sulfanilamide levels double, triple, and even quadruple the accepted therapeutic maximum were recorded. There was frequent overlapping of groups in this respect. This is accounted for on the basis of factors other than volume of Visciadol administered. There was frequent association between high sulfanilamide levels and spillage of Visciadol into the alveoli, ingestion of Visciadol expelled from the lungs by cough, or both. Figure 3

³ This is given as 8 to 10 mg. per cent for "mild" and "moderate" infections (30, 31). Other pharmacology texts give lower levels; in some a blood level of 4 to 6 mg. per cent was recommended (1, 13).

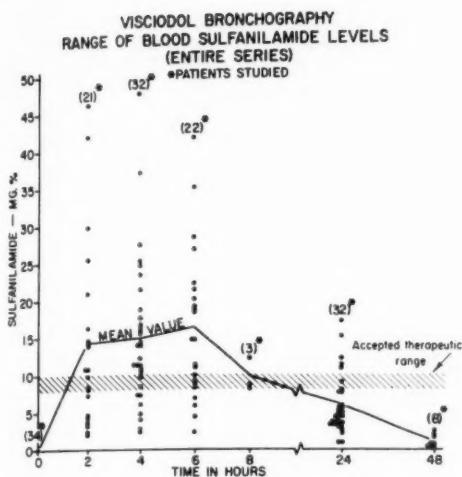


Fig. 2. A plot of all sulfanilamide levels for all patients studied, with mean levels and therapeutic blood sulfanilamide level included for comparison. Numbers in parentheses indicate number of determinations made at the corresponding time.

depicts serial blood sulfanilamide and methemoglobin levels in two patients, each of whom received 13 c.c. of Visciodol at bronchography. In one (Case 28) there had been severe alveolar spillage, and both sulfanilamide and methemoglobin levels were high and sustained. In the other case, a tumor had completely blocked one major bronchus, and elsewhere there was no alveolar spillage; as a result sulfanilamide and methemoglobin levels were very

VISCIODOL BRONCHOGRAPHY Response of 2 patients to an identical volume of Visciodol

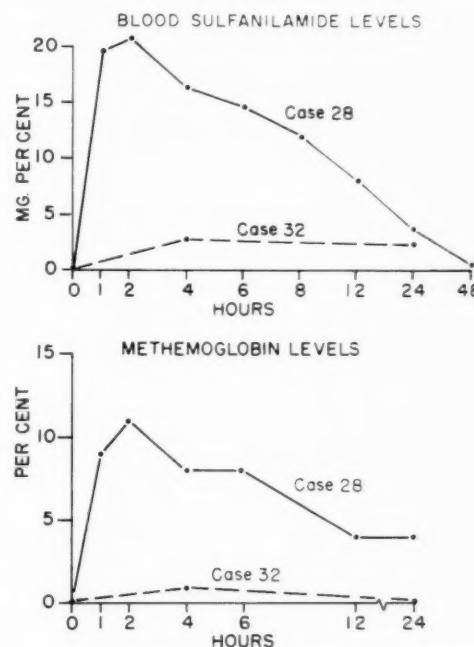


Fig. 3. A comparison of the serial blood sulfanilamide and methemoglobin levels in 2 patients each of whom received 13 c.c. of Visciodol during unilateral bronchography.

low. In Case 1 (See Table I) the highest sulfanilamidemia of the series—47.4 per cent—was seen. This patient had required

TABLE IV: MEAN BLOOD SULFANILAMIDE LEVELS PRODUCED BY VISCIODOL BRONCHOGRAPHY
(All values in milligrams per cent)

	Control Level	Time in Hours After Start of Bronchography					
		2	4	6	8	24	48
Entire Series							
Mean	0	14.1	14.9	16.3	9.6	5.6	0.9
Range	0	2.0-45.8	2.4-47.4	2.3-41.5	8.0-12.0	0.8-17.0	0.0-2.4
(Patients studied)	(34)	(21)	(32)	(22)	(3)	(32)	(8)
Group One							
Mean	0	25.9	24.5	26.5	...	9.7	1.7
Range	0	4.6-45.8	10.1-47.4	8.6-41.5	...	2.6-17.0	1.4-1.9
(Patients studied)	(7)	(6)	(7)	(6)	(0)	(7)	(2)
Group Two							
Mean	0	9.1	14.4	13.7	8.7	5.2	1.2
Range	0	2.3-16.1	4.0-25.0	5.9-22.1	...	0.8-11.8	0.0-2.4
(Patients studied)	(18)	(10)	(17)	(11)	(1)	(17)	(2)
Group Three							
Mean	0	10.1	7.6	9.6	10.0	3.1	0.3
Range	0	2.0-20.8	2.4-16.4	2.3-18.5	8.0-12.0	0.8-5.0	0.1-0.5
(Patients studied)	(9)	(5)	(8)	(5)	(2)	(8)	(4)

a volume of 41 c.c. of Visciodol for unilateral bronchography. Because of poor anesthesia, she had expelled by cough and swallowed an estimated 30 c.c. of this before a satisfactory examination was achieved.

occurred in 7 patients and were associated with cyanosis. As shown in Figure 6 there was a reasonably good correlation between peak individual methemoglobin levels and the corresponding simultaneous blood sulfanilamide levels. The persistence of met-

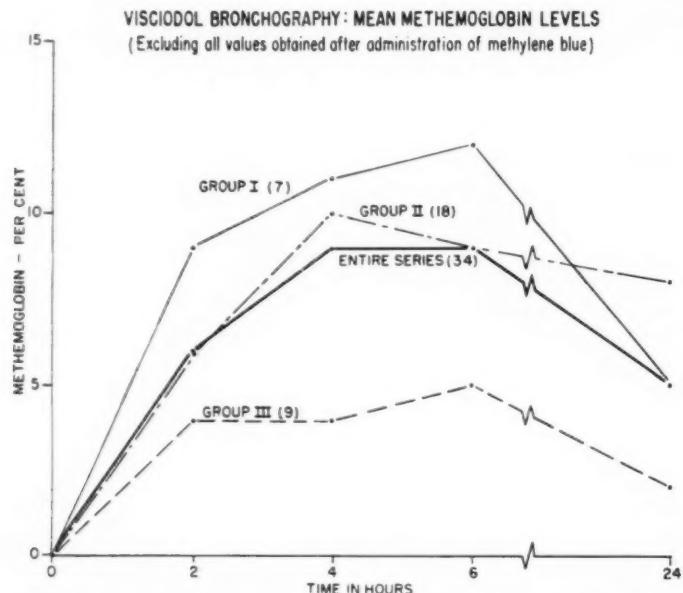


Fig. 4. Graphic demonstration of the magnitude and duration of Visciodol-induced methemoglobinemia for the entire series and its component groups.

Methemoglobin Formation (Table V): All patients were methemoglobin-free before bronchography. Of the thirty-four patients studied, only 5 did not show this ferric blood pigment after administration of Visciodol. Figure 4 illustrates the mean methemoglobin levels for the entire series and its component groups. It is seen that in general the highest methemoglobin levels occurred with the largest doses of Visciodol, but again the factors of alveolar spillage and ingestion of Visciodol expelled from the lungs were important factors. Figure 5 indicates the marked individual variations in peak methemoglobin levels, many of which exceeded the "cyanosis threshold" of 10 to 15 per cent, although the mean levels for the entire series and three component groups did not. Methemoglobin levels in excess of 15 per cent

hemoglobinemia for twenty-four hours or longer after bronchography is consistent with Bodansky's observation that, when produced by a single acute dose of a methemoglobin-forming drug, methemoglobinemia usually requires one to three days for disappearance (2). None of our patients received a methemoglobin-producing compound other than Visciodol.

The occurrence of *high* twenty-four-hour methemoglobin levels in several patients was unexpected. In 1 of 2 patients given methylene blue at twenty-four hours, a drop in methemoglobin level from 11 to 4 per cent was observed. In the second patient (Case 17), however, there was no response to methylene blue administered at twenty-four hours (see Fig. 7). The methemoglobin level of 7 per cent rose to 9 per cent after this therapeutic test, but

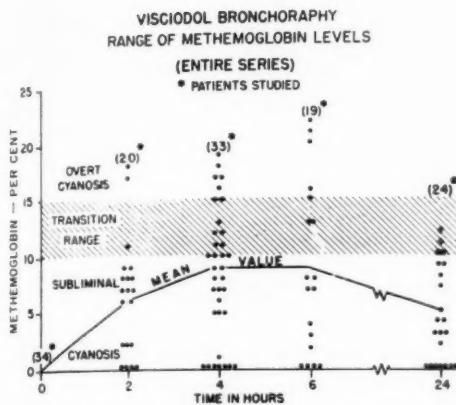


Fig. 5. A plot of all methemoglobin levels in all patients studied. Numbers in parentheses show the number of determinations made at the corresponding time. Hatched line indicates the methemoglobin levels above which cyanosis is clearly seen; levels in the transition range may produce clinical cyanosis.

this rise is not necessarily significant, being still within the limit of error of the method. The possibility exists that this determination was a laboratory error. It is not inconceivable, however, that the pigments sulfhemoglobin and/or choleglobin were present. These pigments have absorption peaks of 620 and 629 m μ , respectively; that

TABLE V: MEAN BLOOD METHEMOGLOBIN LEVELS (IN PER CENT OF TOTAL HEMOGLOBIN) PRODUCED BY VISCIODOL BRONCHOGRAPHY

(Excluding all values obtained after administration of methylene blue)

	Control Level	Time in Hours After Start of Bronchography			
		2	4	6	24
Entire Series					
Mean	0	6%	9%	9%	5%
Range	0	0-18%	0-19%	0-22%	0-15%
(Patients Studied)	(34)	(20)	(33)	(19)	(24)
Group One					
Mean	0	9%	11%	12%	5%
Range	0	0-18%	0-19%	0-22%	0-10%
(Patients Studied)	(7)	(6)	(7)	(6)	(7)
Group Two					
Mean	0	6%	10%	9%	8%
Range	0	0-9%	0-17%	0-20%	0-15%
(Patients Studied)	(18)	(9)	(18)	(9)	(11)
Group Three					
Mean	0	4%	4%	5%	2%
Range	0	0-11%	0-12%	0-8%	0-4%
(Patients Studied)	(9)	(5)	(8)	(4)	(6)

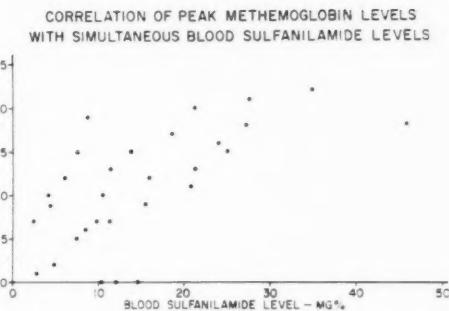


Figure 6

RESPONSE OF METHEMOGLOBINEMIA TO METHYLENE BLUE

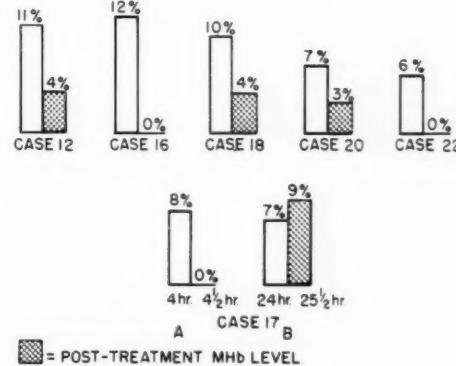


Fig. 7. Graphic presentation of data contained in Table II. The white bars represent pretreatment levels of methemoglobin.

of methemoglobin is 630 m μ (19). The differentiation of pigments spectroscopically similar to methemoglobin was beyond the scope of this investigation. The association of sulfhemoglobin formation following sulfanilamide administration is well known (16). It has been shown that choleglobin may be formed from methemoglobin, and that there is parallelism between the formation of methemoglobin and choleglobin from oxyhemoglobin (20). Further investigation of this possibility would be of interest; in such a study the cyanide conversion method of methemoglobin measurement should be carried out.

Response to Methylene Blue (Table II): Conversion of methemoglobin to hemoglobin depends on reduction of the oxidized iron in heme to its ferrous state. This may

TABLE VI: BLOOD SULFANILAMIDE LEVELS (IN MG. PER CENT) IN DOGS AFTER INTRAGASTRIC AND INTRABRONCHIAL ADMINISTRATION OF VISCIODOL

Control Levels			Hours After Administration				
	1	2	4	6	12	24	48
Intragastric "Viscioldol"							
Dog B	0.2	0.4	1.6	10.0	10.7	..	12.4
Dog C	0.2	1.0	2.6	6.0	7.2	..	20.2
Dog D	0.0	8.0	12.8	18.6	15.7	..	10.1
Mean	0.1	3.1	5.7	11.5	11.2	..	14.2
Intrabronchial "Viscioldol"							
Dog A	0.0	..	25.8	25.0	19.1	14.6	7.9
Dog B	0.0	..	23.1	21.0	21.8	11.1	3.7
Dog C	0.0	19.4	27.6	24.2	16.6	14.8	8.3
Dog D	0.0	21.8	22.1	21.4	20.6	..	10.8
Mean	0.0	20.6	24.7	22.9	19.5	13.5	7.7
							0.9

be accomplished *in vivo* by any of several reducing agents, including ascorbic acid and reduced methylene blue.⁴ In low doses the latter produces conversion rapidly, the effect usually being maximal in thirty to ninety minutes (10, 34). Methemoglobinemia will subsequently recur, however, if the methemoglobin-forming compound remains present in significant amounts.

The therapeutic effect of methylene blue was measured 7 times in 6 patients. In all but one instance the methemoglobin level fell by at least 50 per cent, or disappeared, in thirty to ninety minutes (see Figure 7). The atypical result noted in the seventh therapeutic test (Case 17, B) has been discussed above.

Comparison of Gastrointestinal and Bronchial Absorption of Sulfanilamide (Table VI): In order to isolate and evaluate the magnitude of sulfanilamide absorption from the bronchi and from the gastrointestinal tract, several studies were carried out in anesthetized dogs. Human subjects were not used, since prolonged anesthesia was necessary to prevent "contamination" of the route under investigation, either by ingestion of intrabronchial Visciodol after cough or by aspiration of intragastric Visciodol after possible emesis. The results of this portion of the investigation, shown

in Figure 8, demonstrate that, under the experimental conditions, sulfanilamide was absorbed much more efficiently through the lungs than through the gastrointestinal tract. The effect of dehydration during the period of anesthesia was identical in the two groups.

DISCUSSION

This investigation has demonstrated that bronchography with Visciodol in accepted doses invariably produces sulfanilamidemia, the magnitude of which is dependent upon the volume given, on the degree of alveolar spillage, and on the amount which is ingested. This sulfanilamidemia exceeds the therapeutic blood sulfanilamide level and persists for at least twenty-four hours and usually forty-eight. There is in most instances an associated methemoglobinemia which may reach cyanotic levels.

It is well known that the occurrence of serious side-reactions to sulfanilamide is unpredictable and bears no constant relation to dose or even to blood levels (31). For this reason, there has never been a "safe" or "nontoxic" dose of sulfanilamide. Nevertheless it has been recently stated, with respect to Visciodol, that "the amount of sulfanilamide used for a bronchogram is safe" (7). According to the same source, "the sulfanilamide content (of Visciodol) is considerably less than any therapeutic—not to say toxic—dose."

Sulfanilamide was for all practical purposes discarded as a therapeutic agent over

⁴ Within the erythrocyte methylene blue undergoes reduction to leuko-methylene blue (methylene white); this reaction is mediated by one or more enzyme systems. Leuko-methylene blue is the active reducing agent.

a decade ago, because of the high incidence of fatal, major, and minor reactions associated with its use (14). It is true that acute sulfanilamide administration, as during Visciodol bronchography, is not analogous to chronic therapeutic administration. However, even acute administration has produced fatalities. A death has been reported (21) following a single dose of 300 mg. of sulfanilamide—the amount contained in 1.0 c.c. of Visciodol. A fatal case of acute hemolytic anemia has been described, occurring after administration of 10 gm. of sulfanilamide in less than one day (32). A comparable dose is contained in 32 c.c. of Visciodol.

To date, however, no fatality attributable to the bronchographic use of Visciodol, or its European precursor, Lipiodol-sulfanilamide, has been reported or is known to the manufacturer (11). Since well over 10,000 bronchograms have been obtained in Europe with the latter medium and nearly 1,000 bronchograms in America with Visciodol, it is safe to conclude that the risk of a fatal sulfanilamide reaction precipitated by the use of this medium is of very low magnitude. It cannot, however, be said to be nonexistent, since Lipiodol itself has been implicated in post-bronchography deaths (26). Unless it is assumed (no basis for such an assumption is known to the authors) that the presence of powdered sulfanilamide "protects" the patient against a Lipiodol-induced fatality, the reasonable conclusion is that the number of Visciodol and Lipiodol-sulfanilamide bronchograms is still too small to reflect the inherent associated mortality. Despite the popularity of aqueous and oily Dionosil, Lipiodol is still used five times as frequently as Visciodol and Lipiodol-sulfanilamide for bronchography (26).

There is another major hazard temporally separated from, but nevertheless related to, sulfanilamide administration. This is the development of hypersensitivity to sulfonamide, which remains latent until a second exposure to the drug precipitates an overt clinical reaction. Sulfonamide hypersensitivity has been postulated by

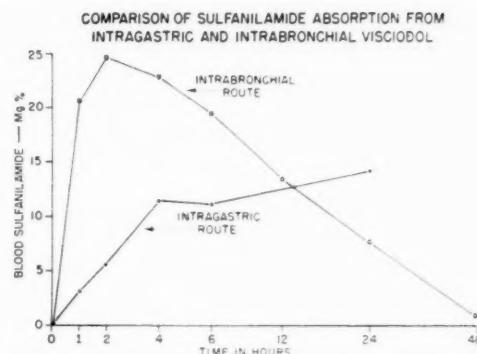


Fig. 8. Graphic presentation of data contained in Table VI. Each curve is constructed from mean levels for the particular animal group.

several investigators as an etiological factor in the so-called "collagen diseases," particularly systemic lupus erythematosus and periarteritis nodosa (17, 27, 28). Many physicians today consider this to be a contraindication to the use of sulfonamides whenever another drug may be employed.

Methemoglobin is not toxic *per se* except in high concentration, but it reduces the body store of functioning hemoglobin and thus impairs oxygenation of the tissues (3). Further, the oxyhemoglobin dissociation curve is "shifted to the left" and distorted by methemoglobinemia, reflecting reduced ability of oxyhemoglobin to unload oxygen at the tissue level. Chemically induced methemoglobinemia has been shown to impair oxygenation of muscle in human volunteers, thus requiring earlier and greater use of anaerobic (glycolytic) oxidation systems for energy supply. In man, conversion of 10 per cent of a normal amount of hemoglobin to methemoglobin produces borderline cyanosis, which becomes readily apparent at levels of 15 per cent. When levels exceed 30 per cent, progressive dyspnea ensues, followed by lethargy and semistupor. In animals levels above 40 per cent produce an increased cardiac output, apparently in response to tissue anoxia (3). The patient with chronic respiratory insufficiency or with severe coronary insufficiency may not be able to tolerate the additional burden imposed by augmenta-

tion of his hypoxemia during transient methemoglobinemia. Finally, it is possible to confuse methemoglobin cyanosis with that caused by anoxia, creating the possibility of alarm on the part of both physician and patient when oxygen fails to clear the cyanosis.

In forming a value judgment on Visciodol as a bronchographic agent, consideration must be given to its advantages as well as the disadvantages which have been outlined. Visciodol does produce bronchograms of high diagnostic quality, it does undergo rapid expulsion from the lungs, and it does infrequently penetrate the alveoli. The question is not whether high-viscosity bronchographic agents are desirable, but whether a *specific* high-viscosity agent—Viscioldol—shown to have potentially hazardous effects, should continue to be used because it also has desirable properties. Each physician who contemplates using Visciodol must answer this question for himself. On the basis of this investigation it is our conclusion that the use of Visciodol adds a small—but unjustifiable—risk to bronchography, because of its sulfanilamide content. This risk is unjustifiable because it is an *avoidable* one, optionally assumed, in contrast to the unavoidable risks inherent in administration of iodinated media and local anesthetics.

The need is for preservation of the desirable properties of high-viscosity contrast media by substitution of a pharmacologically and physiologically inert viscosing agent. Viscosing agents other than sulfanilamide have been used but cannot be considered inert (15, 29).

It is realized that not all physicians who perform bronchography may wish to discard Visciodol before a safe substitute becomes available. Therefore, the following recommendations for the use of Visciodol are submitted:

1. Visciodol should not be employed when the patient gives a history of sulfanilamide reaction, or when an adequate history cannot be obtained.

2. The patient should be carefully in-

structed to avoid swallowing any material that may be expelled by cough during or after Visciodol bronchography.

3. Visciodol should not be used in patients whose cough cannot be suppressed or who cannot cooperate. In such patients the likelihood of ingestion of Visciodol is increased.

4. Dosage of Visciodol should be kept as low as possible. Preheating is inadvisable, for the reduction in viscosity increases the likelihood of alveolar penetration; this in turn enhances sulfanilamide absorption.

5. If Visciodol bronchography is contemplated in patients with respiratory insufficiency, consideration should be given to prophylactic pretreatment with methylene blue to minimize methemoglobin formation.

6. Cyanosis occurring after Visciodol bronchography should be considered due to methemoglobinemia unless there are compelling signs of another cause, such as atelectasis. Intravenous administration of a 1 per cent aqueous solution of sterile methylene blue, in dosage of 1.0 to 2.0 mg. per kilogram of body weight, is both a therapeutic test and the treatment of choice.

SUMMARY

Thirty-five patients were studied for sulfanilamide absorption and methemoglobin formation after bronchography with Visciodol. Dosages of the contrast medium were comparable, in all but one case, to those used by most bronchographers. Sulfanilamidemia occurred invariably, the mean blood sulfanilamide level exceeding the accepted therapeutic range during the second to sixth post-bronchography hours. In general, the higher blood sulfanilamide levels occurred with use of larger volumes of Visciodol. Methemoglobin formation occurred in 29 patients, and produced overt cyanosis at higher levels. Both alveolar spillage and Visciodol ingestion enhanced blood sulfanilamide and methemoglobin values. Visciodol studies in animals indicated greater absorption of

sulfanilamide from the lungs than from the gastrointestinal tract. Methylene blue proved effective in reducing blood met-hemoglobin levels.

The immediate and delayed hazards of sulfanilamide administration have been discussed, and it is concluded that the use of Visciodol carries a small but unjustifiable risk. Certain recommendations are made for those physicians who may continue to use this medium.

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SUMMARIO IN INTERLINGUA

Un Evalutation del Hazardos Pharmacologic que Resulta ab le Uso
de "Visciодol" in le Bronchographia

Trenta-cinque patientes esseva studiate pro absorption de sulfanilamido e formation de methemoglobin post bronchographia a Visciodol. Le doses del substantia de contrasto usate esseva simile, in omne le casos con un exception, al doses usate per le majoritate del bronchographos. Sulfanilamidemia occurreva invariabilmente; le concentration medie de sulfanilamido in le sanguine excedeva le acceptate nivellois therapeutic durante le periodo ab le secunde usque al sexta hora post-bronchographic. A generalmente parlar, le plus alte nivellois de sulfanilamido in le sanguine occurreva con le uso de plus grande volumines de Visciodol. Formation de methemoglobin occurreva in 29 patientes e produceva cyanosis patente al nivellois plus elevate. Tanto le effusion de Visciodol ab le alveolos e le ingestion de illo accentuava le valores de sulfanilamido

sanguinee e de methemoglobin. Studios con Visciodol in animales experimental revelava plus alte grados de absorption de sulfanilamido ab le pulmones que ab le vias gastro-intestinal. Blau methylenic se provava efficace a reducer le nivellois de methemoglobin in le sanguine.

Le hasardos immediate e tardive del administration de sulfanilamido es discutite. Como agente therapeutic, sulfanilamido esseva rejicite plus que un decennio retro a causa del reactiones major e minor e mortal que esseva associate con su uso. Ben que nulle mortes attribuibile al uso de Visciodol in bronchographia ha essite reportate, le autores opina nonobstante que su contento de sulfanilamido constitue un risco que es micre sed que non pote esser justificate.

Certe recommendations es facite pro medicos qui continua le uso de iste substantia.



Barium Sulfate and Bismuth Subcarbonate Suspensions as Bronchographic Contrast Media¹

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DURING THE LAST five years several papers have appeared concerning the advantages and disadvantages of the various bronchographic contrast media which contain iodine as the radiopaque ingredient. While these media are relatively safe, as manifested by their extensive clinical use, it is nevertheless recognized that an occasional individual is dangerously sensitive to organic iodine compounds. Furthermore, the oily iodine-containing media are known to produce chronic lipoid pneumonia and granulomata in certain patients. Aqueous suspensions are available, but it has become apparent to us that these are more irritating to the tracheobronchial mucosa than are the oily media. In recent years sulfanilamide has been added to Lipiodol in order to hasten removal (absorption) of the iodine from the lung. However, the known hazards of sulfanilamide, when added to those of iodine, would seem to preclude the acceptance of such a medium as the ideal contrast material. On the other hand, aqueous suspensions of barium sulfate are known to be pharmacologically inert and of excellent radiographic density. Theoretically, at least, the use of barium sulfate in the tracheobronchial tree would eliminate the undesirable sequelae which are associated with the various iodine-containing compounds. It is the purpose of the present paper to report the results of an investigation of the use of barium sulfate and bismuth subcarbonate suspensions in the tracheobronchial tree, first in animals and subsequently in man.

Certain clinical observations and good-natured debate with clinical colleagues were partly responsible for the decision to make a serious study of the use of barium sulfate as a bronchographic contrast material. It is known that patients occasion-

ally aspirate ordinary aqueous suspensions of barium sulfate when they swallow these media during roentgenologic study of tracheo-esophageal fistulae, neurologic disturbances in deglutition, and obstructing lesions of the upper esophagus. As most of us realize, when these inadvertent aspirations of barium sulfate occur, the aspirated barium almost invariably disappears from the tracheobronchial tree after a few hours, or at the maximum two or three days, and without the slightest evidence of any deleterious effect on the patient. Nevertheless, the fear of aspiration of barium is so prevalent among our nonradiological colleagues that they frequently demand that their patients be examined with iodized oil if there is even a remote possibility of aspiration. This is usually disagreeable to the patient, expensive, often diagnostically unrewarding to the radiologist, and probably unnecessary in view of the absence of undesirable clinical sequelae following barium aspiration.

Of all the suspending agents available for making a barium mixture of the proper viscosity for contrast study of the tracheobronchial mucosa, carboxymethylcellulose was the best understood and seemed the most logical choice. This material is ingested by the public in ice cream, jams, jellies, and canned fruit because of its desirable water-solubility and viscosity-producing properties. It is already used in a wide variety of barium preparations for gastrointestinal radiology and is also employed to increase the viscosity of certain water-soluble iodine-containing bronchographic contrast media. Most investigators (1, 4, 5, 6, 9) believe carboxymethylcellulose to be innocuous in the lung, while others (2, 3) temper any tendency to over-

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ANIMAL EXPERIMENTATION

CONTRAST MEDIUM	NUMBER OF ANIMALS (RABBITS)	PATHOLOGICAL CHANGES			RETAINED CONTRAST		
		24 HRS	1 WK	2 1/2 MONTHS	24 HRS	1 WK	2 1/2 MONTHS
DIONOSIL	7	3/3	2/2	0/2	3/3	2/2	0/2
BARIUM SULFATE	6	2/2	2/2	0/2	2/2	2/2	0/2
LIPIODOL	7	3/3	2/2	0/2	3/3	2/2	0/2
BISMUTH SUB-CARBONATE	4	1/1	1/1	2/2	1/1	0/1	0/2

Fig. 1. Table showing the incidence of histopathologic changes and retention of contrast material in four groups of animals, each group having received trans-tracheal injections of one of the four contrast materials used in this experiment. The denominators in the "fractions" denote the number of animals studied at the indicated time intervals; the numerators the number of animals with histopathological changes or retained contrast material; e.g., 2/3 means "two out of three."

enthusiasm with the admonition that large amounts can produce pulmonary fibrosis. We concluded that this material would be safe, although we determined to study histologic specimens carefully for any evidence of permanent changes due either to carboxymethylcellulose or barium sulfate in animals, and, if feasible, later in man. We believed that, even if there were minimal evidence of pulmonary fibrosis in animals, this possibility would probably be almost completely eliminated in man, since patient co-operation allows the bulk of the injected contrast material to be recovered from the tracheobronchial tree. Furthermore, proper viscosity of the contrast material should preclude its passage into the tiny bronchioles and alveoli. If minimal amounts of carboxymethylcellulose did reach the alveoli, it would most likely become phagocytized, or otherwise absorbed, and safely eliminated *via* the kidneys (8).

We have only recently noted with great interest that Di Rienzo (9) in Argentina also has reported the use of carboxymethylcellulose suspensions of barium sulfate for bronchographic contrast examination. He makes no mention, however, of any histopathologic or physiologic studies, either in animals or man, which we believe are necessary from scientific and medicolegal standpoints before any large scale clinical studies should be confidently undertaken. Skinner *et al.* (10), at the recent meeting

of the American Roentgen Ray Society in Washington, D. C., reported their work comparing the histopathologic effects of injections of Aqueous Dionosil, Lipiodol, and barium sulfate into the tracheobronchial tree of rats. They concluded that Aqueous Dionosil caused the greatest cellular exudative response but led to the least permanent changes. Lipiodol produced the most fibrosis, whereas barium sulfate was retained in the lung longer than Aqueous Dionosil and Lipiodol. We do not know how to correlate their as yet unpublished work in rats with our studies in rabbits and later in man.

ANIMAL EXPERIMENTAL STUDIES

In view of the theoretical danger of chronic pulmonary damage, such as fibrosis or some type of pneumoconiosis, it was decided to undertake an evaluation of the histologic and physiologic effects of the media to be studied in animals before using them routinely in man.

As shown in Figure 1, four groups of rabbits were used for parallel studies on Dionosil Oily, Lipiodol, bismuth subcarbonate, and barium sulfate. The barium-sulfate suspension consisted of one part by weight of Micropaque² and two parts by weight of a solution of normal saline containing 1.5 per cent sodium carboxymethylcellulose.³ Micropaque barium powder contains 92 per cent barium sulfate, 5 per cent lactose, and 3 per cent water-soluble organic material consisting of flavoring and "agglutinating materials" of unknown composition, but apparently without any significant physiologic effects as determined by our histopathologic studies. Other proprietary mixtures of barium sulfate and suspending agents would probably be equally satisfactory, inasmuch as they probably contain similar pharmacologically inert suspending agents. However, since

² Micropaque is distributed in the United States by the Picker X-ray Corporation by arrangement with the manufacturers, Damancy & Co., Ltd., Ware, Herts, England.

³ Sodium-carboxymethylcellulose, Type 70, High Viscosity (Lot No. 4452), manufactured by Hercules Powder Co., Wilmington, Delaware.

each proprietary preparation contains unknown ingredients, each must be tested in animal bronchography before it can be assumed to be safe in man.

Animals from each of the four groups were sacrificed at intervals of twenty-four hours, one week, and ten weeks following the administration of the contrast material transtracheally with a hypodermic needle. One and one-half cubic centimeters of the medium was injected at room temperature into the trachea of each animal. Each rabbit weighed approximately 5 pounds. Chest films were obtained after each injection to confirm the filling of the lower lobe bronchi and to follow elimination of the contrast material. The following histopathologic observations were made:

I. *Twenty-four Hours:* (a) *Dionosil Oily:* Two animals were sacrificed. In each the bronchioles were generally empty and not remarkable. There was, however, extensive edema in the alveolar spaces, having a vacuolated appearance presumably due to the presence of lipid-containing material from the Dionosil. The pulmonary capillaries were somewhat congested.

(b) *Lipiodol:* Two animals were sacrificed. Sections from each showed the tissue to be poorly fixed, presumably because of lack of infiltration of the fixing fluid into the area containing the oily solution. There were numerous inflammatory cells in the alveolar spaces, including both macrophages and leukocytes. Occasionally the cytoplasm of macrophages contained rather large vacuoles.

(c) *Bismuth subcarbonate:* One animal was sacrificed. Sections showed many terminal bronchioles filled with polymorphonuclear leukocytes and fluid, intermixed with which were innumerable particles of dense opaque black material (bismuth). The greater part of this material appeared to be extracellular, with a few particles having been phagocytized by the leukocytes.

(d) *Barium sulfate:* Two animals were sacrificed. Sections of each showed the majority of the bronchioles in the lower lobes to be filled with polymorphonuclear leukocytes and fluid intermixed with numerous opaque particles of barium. Many of the particles were suspended free in the fluid, while others had been phagocytized by the leukocytes. Frequently particles of barium were present in the lumina of the bronchioles, respiratory bronchioles, alveolar ducts, and alveolar spaces, the response to the material being similar everywhere.

II. *One Week:* (a) *Dionosil:* Two animals were sacrificed. The pulmonary tissue was generally air-containing and most of the bronchioles were empty.

An occasional bronchiole contained a small amount of somewhat eosinophilic material with vacuoles suggesting lipid droplets. There was slight generalized diffuse lymphocytic infiltration of alveolar walls with slight thickening.

(b) *Lipiodol:* Two animals were sacrificed. The tissue in each was well fixed. In one of the animals the bronchioles and alveoli were generally empty, while in the other there were moderately excessive numbers of macrophages in the lumen of alveoli and respiratory bronchioles. The cytoplasm of these cells contained occasional vacuoles.

(c) *Bismuth subcarbonate:* One animal was sacrificed. Sections showed rather extensive areas of consolidation of the pulmonary tissue by infiltrating polymorphonuclears, lymphocytes, and macrophages. The greater part of the bismuth had accumulated into dense foci within the areas of general consolidation. However, there were minute isolated particles widely distributed throughout the area of infiltration. Lymphocytic infiltration was present throughout, partially obscuring the alveolar spaces. Those which were recognizable were lined by hypertrophied epithelium.

(d) *Barium sulfate:* Two animals were sacrificed. Sections of one of these animals showed extensive areas of consolidation of the alveolar spaces by large pale macrophages, the cytoplasm of which was packed with particles of barium sulfate. In areas of extensive consolidation occasional multinucleated giant cells were seen, and there was evidence of hypertrophy of the alveolar epithelium. There was also slight lymphocytic infiltration of the alveolar septa, which were slightly thickened in these areas. In smaller foci of consolidation the alveoli were somewhat collapsed and filled with phagocytic cells, but there was no evidence of epithelial reaction or alveolar septal thickening. The second animal showed only small foci of consolidation of perhaps ten or twelve adjacent alveolar spaces with large pale macrophages. There was no evidence of infiltration into alveolar walls or thickening of these walls.

III. *Ten Weeks:* (a) *Dionosil:* Two animals were sacrificed. Neither one showed recognizable residual histopathologic or intraluminal evidence of the experimental procedure.

(b) *Lipiodol:* Two animals were sacrificed. Sections of each failed to show histopathologic or intraluminal evidence of the experimental procedure.

(c) *Bismuth subcarbonate:* Two animals were sacrificed. The greater part of the bismuth appeared to have been removed from the lungs of these animals. There were scattered foci, however, in which the material was still present. It is apparent that these foci represented sites in which phagocytic cells containing the particles had infiltrated into the stromal tissue of the lungs in the region of bronchioles and perivascular tissues. In such sites of localization there were some necrotic tissue and dense lymphocytic infiltration.

(d) *Barium sulfate:* Two animals were sacrificed.

PATIENTS' REACTION TO BRONCHOGRAPHY

	with BaSO ₄	with DIONOSIL
TOTAL NUMBER OF EXAMINATIONS	50	50
TEMPERATURE ELEVATION IN 24 HRS. (ABOVE 38°). NO. OF CASES	10	10
TEMPERATURE ELEVATION FOR MORE THAN 24 HRS. NO. OF CASES	0	4
INCREASED PULSE RATE IN 24 HRS. (ABOVE 100). NO. OF CASES	11	23
INCREASED PULSE RATE FOR MORE THAN 24 HRS. NO. OF CASES	5	6

IN NONE OF THE CASES DID ELEVATED TEMPERATURE OR ELEVATED PULSE RATE LAST FOR MORE THAN 3 DAYS.

Fig. 2. Response of temperature and pulse rate in 100 patients who underwent bronchography, 50 patients having received barium sulfate as the contrast material, the remaining 50 patients having received Dionosil Oily.

Neither showed the slightest evidence of the opaque material or significant tissue reaction anywhere in the sections prepared.

**CONCLUSIONS BASED UPON EXPERIMENTAL
ANIMAL DATA**

It is of interest that we were unable to show any significant histopathological differences in the acute effects of the four contrast media. The histopathologic response was predominantly a foreign-body reaction. The most intense and prolonged reaction was that seen in the lungs following the use of bismuth subcarbonate. With this medium definite abnormal histopathologic changes were still obvious at ten weeks. Some phagocytized bismuth, with infiltration of the phagocytes into the peri-bronchial and perivasculär tissues, was seen in two animals studied at that interval. It was therefore decided to abandon the use of bismuth subcarbonate. We were unable to find any permanent histopathologic effects of Dionosil Oily, Lipiodol, or barium sulfate at ten weeks. Nor did we observe any evidence of residual intra-alveolar Dionosil, Lipiodol, or barium at that time. We believe that the absence of any fibrotic reaction should preclude the theoretical danger of a pneumoconiosis due to the aspiration of aqueous suspensions of barium sulfate.

It was somewhat disconcerting to us

that we did not note histopathologic abnormalities or retained Lipiodol or Dionosil Oily in those rabbits sacrificed at ten weeks, inasmuch as Björk and Lodin (11) found oil residua from Dionosil Oily in 8 of 10 rabbits at the end of three months, and 3 of these 8 had a few small foreign body granulomata. It is possible that we might have found similar abnormalities had we used more animals, but it is also possible that these investigators warmed the oily contrast material before injection and thus obtained a greater degree of alveolar filling than when the materials are injected at room temperature, as in our experiment. Because of this discrepancy, we were somewhat relieved to read the recent report by Holden and Cowdell (12), who were unable to substantiate in man the late effects of Dionosil Oily reported by Björk and Lodin. Holden and Cowdell attributed this to anatomical and physiological differences between rabbit and man. Also, the undesirable sequelae due to retention of the medium following bronchography are minimized in man because there is usually considerable success in recovering most of the contrast material from the bronchial tree. In spite of the aforementioned discrepancy, therefore, we did not believe it was necessary to prolong our comparative animal experiments.

**CLINICAL EVALUATION OF
BARIUM-SULFATE BRONCHOGRAPHY**

In our clinical investigation of the use of barium sulfate as a bronchographic contrast medium, we recorded in every patient the response of the temperature and pulse after bronchography, assuming that these vital signs would be good indices of the patient's reaction to the pharmacologic or inflammatory effects of the injected medium. Fifty patients in whom barium sulfate was used were compared with a parallel group of 50 patients receiving Dionosil Oily, the latter contrast material, in our opinion, being the best of the iodine-containing contrast media available to date. Figure 2 shows a comparison of the temperature and pulse responses following

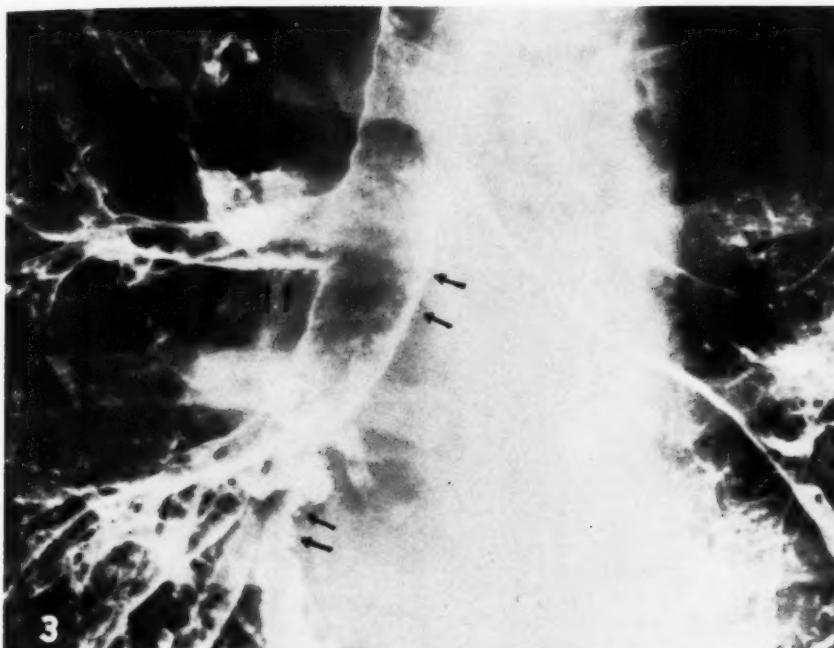


Fig. 3. Enlarged view of larger bronchi showing filling of the dilated bronchial mucosal glands with barium sulfate (arrows), indicative of chronic bronchitis in the inferior aspect of the right upper lobe bronchus and posterior basal segmental branches of the right lower lobe.

the use of Dionosil Oily and barium sulfate. Twenty-three of 50 patients had a pulse rate above 100 per minute within twenty-four hours following Dionosil bronchography, whereas only 11 out of 50 showed a similar pulse rate elevation following the use of barium sulfate. In each group there were 10 patients in whom the temperature rose above 38° C. within twenty-four hours after bronchography. No patient in whom we used barium sulfate exhibited a temperature elevation of more than twenty-four hours duration, whereas 4 of the 50 who had received Dionosil still showed temperatures above normal beyond that period. In none of the patients, regardless of which contrast medium was used, did the rise in temperature or increase in pulse rate persist for more than three days.

Radiographic contrast was excellent with barium sulfate, which was to be expected, inasmuch as the atomic number of barium is 56 and its atomic weight 137, in contrast to an atomic number of 53 and atomic

weight of 126 for iodine. Furthermore, the coating of the bronchial mucosa was excellent. The suspending materials almost completely prevent alveolization of the contrast medium and result in uniform mucosal coating. In order to preclude further the unnecessary alveolization and possible retention of the contrast medium, postural drainage was used and a moderate amount of coughing encouraged in order to raise as much of the contrast medium as possible as soon as the bronchogram was completed. Retention of the barium-sulfate medium due to alveolization was thus greatly minimized. Furthermore, our studies in rabbits indicated that even when the contrast medium was intentionally alveolized (due to flooding the bronchi with the medium), there was, nevertheless, no residual barium detectable histologically ten weeks later. We placed 1.5 c.c. of barium mixture in the lower lobes of 5-pound rabbits, which is the equivalent of 45 c.c. placed in the lower



Fig. 4. Bronchograms obtained with barium-sulfate in a patient with right upper lobe tuberculosis. Note excellent contrast and absence of alveolar filling in spite of the good filling of the terminal bronchi.



Fig. 5. Barium-sulfate bronchogram in patient with right upper lobe tuberculosis. Note good delineation of the right tracheobronchial tree and the absence of alveolarization in spite of filling of the terminal bronchi. This is particularly well demonstrated in the left lower lobe.

lobes of a 150-pound man. Histologic sections showed alveolar filling as previously described.

All types of pathology are easily demonstrated. For instance, the dilatation of the tiny bronchial mucosal glands can be clearly seen in patients with chronic bronchitis (Fig. 3). To be noted is the consistent lack of alveolarization of the barium suspension, in spite of good filling of the smaller bronchioles (Figs. 4-6). This we attribute to the viscosity of the contrast material and good anesthesia, which prevents vigorous coughing during the procedure. The barium is almost never visible on films after twenty-four hours. Even when barium sulfate entered cysts and/or diseased bronchi, it was eliminated rapidly (Fig. 7). In 47 out of 50 patients there was complete disappearance of the contrast material within seven days as judged by post-bronchography chest films, most of the patients showing no residual barium after twenty-four hours.

In 3 patients out of 50 there was a prolonged retention of some of the barium sulfate in the pulmonary parenchyma. These patients were among the earliest studied, and the suspension used was made with saline which contained only 0.5 per cent sodium carboxymethylcellulose in-

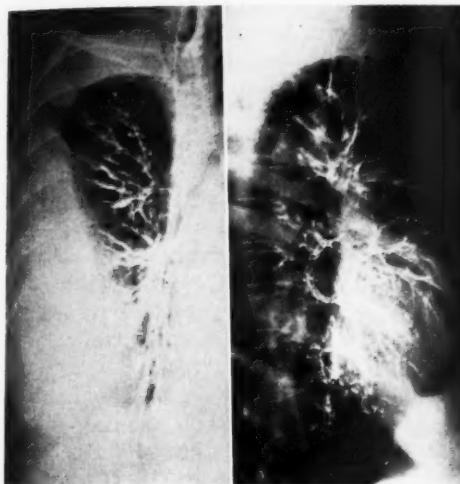


Fig. 6. Barium-sulfate bronchogram in patient with large right-sided tuberculous pleural effusion. Contrast is good in spite of the large amount of fluid in the right hemithorax.

stead of 1.5 per cent subsequently employed. Furthermore, these patients were extremely emphysematous, which condition almost certainly favors the retention of any contrast material, regardless of type. Although, in general, it is probably best to omit bronchography in severely emphysematous patients if permanent reten-

HISTOLOGIC CHANGES IN RESECTED LUNG SPECIMENS IN FIFTEEN PATIENTS WHO HAD DIONOSIL BRONCHOGrams PRIOR TO SURGERY...

TIME INTERVAL BETWEEN BRONCHOGRA- PHY AND RE- SECTION	NUMBER OF PATIENTS	MICROSCOPIC CHANGES ATTRIBUTED TO DIONOSIL OILY.
0-4 WEEKS	7	1 CASE WITH INTENSE DIFFUSE LIPOID PNEUMONIA (3.5 WEEKS).
4-8 WEEKS	5	3 CASES IN WHICH SMALL FOCI OF LIPOID PNEUMONIA OR DROPLETS OF RESIDUAL OIL, WERE FOUND.
8 WEEKS- 6 MONTHS	3	NONE

Fig. 8. Histopathologic changes in resected lung specimens of 15 patients following Dionosil Oily bronchograms.

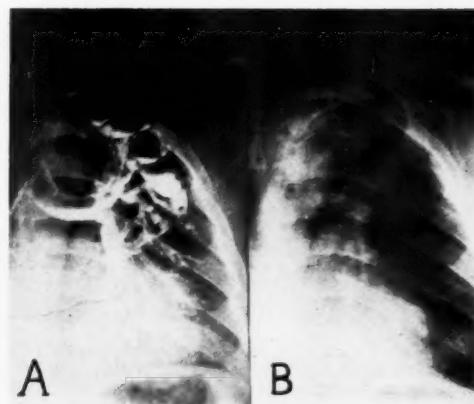


Fig. 7. A. Barium-sulfate bronchogram demonstrating several cystic lesions in the left upper lobe. B. Chest film made less than twenty-four hours later demonstrates complete disappearance of the contrast medium.

tion of the contrast material is to be avoided, it is nevertheless probable that prolonged retention of barium-sulfate suspensions is no more likely than is prolonged retention of any other contrast medium yet available.

COMPARATIVE HISTOPATHOLOGIC STUDIES FOLLOWING BRONCHOGRAPHY WITH BARIUM SULFATE AND WITH DIONOSIL OILY

Figure 8 is a tabulation of the data obtained by studying the resected lung specimens in 15 patients in whom bronchography was done with Dionosil Oily prior to pulmonary resection for a variety of lesions, chiefly tuberculosis. Four of 12

HISTOLOGIC CHANGES IN RESECTED LUNG SPECIMENS IN FIFTEEN PATIENTS WHO HAD BARIUM-SULFATE BRONCHOGrams PRIOR TO SURGERY...

TIME INTERVAL BETWEEN BRONCHOGRA- PHY AND RE- SECTION	NUMBER OF PATIENTS	MICROSCOPIC CHANGES ATTRIBUTED TO BARIUM SULFATE
0-4 WEEKS	6	4 CASES IN WHICH BARIUM SULFATE PARTICLES WERE SEEN IN ALVEOLAR CLUMPS IN ALVEOLI OR IN INTERALVEOLAR SEPTA AND FIBROSIS.
4-8 WEEKS	5	NONE
8 WEEKS- 6 MONTHS	4	NONE

Fig. 9. Histopathologic studies of resected lung specimens of 15 patients following barium-sulfate bronchograms.

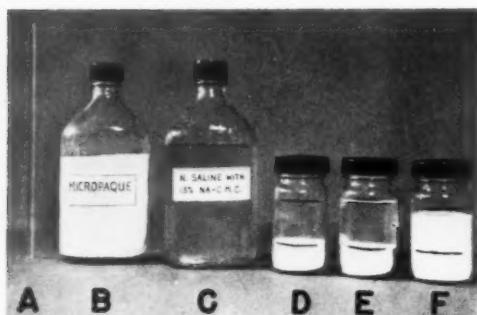


Fig. 10. Preparation of contrast material. (A) Glass stirring rod. (B) "Micropaque" barium powder. (C) Saline-carboxymethylcellulose solution. (D) Mixing bottle in which has been placed 20 gm. of barium powder. Lower mark is made to indicate amount of barium powder to be added when mixing contrast medium for subsequent bronchograms. (E) Mixing bottle following addition of 40 c.c. of saline-carboxymethylcellulose solution to the barium powder. The upper mark is made to indicate the amount of saline-carboxymethylcellulose to be added to the barium powder for subsequent bronchograms. Note that no mixing of barium powder and saline-carboxymethylcellulose solution has occurred. (F) Appearance of contrast material after stirring with the glass stirring rod. After the bottles are marked, the entire procedure takes only a few minutes, and can be carried out by a technician. Once a uniform mixture has been achieved, the contrast material will remain uniformly suspended for many hours.

patients from this group in whom resective surgery was done within eight weeks had evidence of lipoid pneumonia in normal lung tissue adjacent to the pathological lesion. No histopathologic changes which could be attributed to the contrast material were seen in the normal tissues of the resected lung specimens in 3 patients who underwent surgery from eight weeks to six months after the Dionosil Oily bronchography.

As seen in Figure 9, in a group of 15 patients who had resections after barium-sulfate bronchography, 4 of 6 lung specimens resected within four weeks showed residual barium-sulfate particles in the alveoli or in the alveolar septa. No residual barium sulfate could be detected in 9 patients in whom resections were done at intervals from four weeks to six months. In none of the 30 lung specimens studied, regardless of whether Dionosil Oily or barium sulfate was used, was any fibrosis or other pathologic change noted.

METHOD OF PREPARATION OF THE BARIUM-SULFATE SUSPENSION

In order to preclude the necessity for weighing out barium and measuring volumetrically the 1.5 per cent carboxymethylcellulose in normal saline for each bronchogram, we have used small labeled bottles which are marked in such a way (Fig. 10) that barium and the carboxymethylcellulose saline solution can be added together in the proper proportions without resorting to the use of volumetric flasks or scales. We have found that 20 gm. of Micropaque powder and 40 c.c. of normal saline containing 1.5 per cent carboxymethylcellulose provides about 50 c.c. of the suspension, which amount was always adequate for a bilateral bronchogram. It is necessary to add the saline solution to the dry Micropaque barium powder rather than the reverse. The mixing should be accomplished by moderately vigorous stirring with a glass rod, rather than by shaking, if the most homogeneous suspension is to be achieved. No heating or refrigeration is necessary, all mixing being performed at room temperature. Hospital pharmacists can make up any desired volume of saline containing 1.5 per cent carboxymethylcellulose; we have found that 8-ounce bottles can be used conveniently for approximately six bronchograms. If this material is to stand unused for more than a few days, it would probably be wise to add tiny amounts of antibacterial preservatives, although we have not found this necessary in view of a rather large volume of bronchographic work. While most of our work was done with 1.5 per cent sodium carboxymethylcellulose, we believe that 2 or 3 per cent would be desirable. The resulting increase in viscosity should even further preclude the possibility of alveolization of the contrast material.

CONCLUSIONS

Experiments first in rabbits and subsequently in man show that barium sulfate (Micropaque) suspended in normal saline

which contains at least 1.5 per cent sodium carboxymethylcellulose is a safe bronchographic contrast material. There is an early nonspecific foreign-body reaction to this suspension of barium sulfate, as with all other media tested. There was no evidence of sensitivity. Barium-sulfate bronchography in 50 patients was attended by fewer instances of temperature and pulse elevation than were observed in a parallel group of 50 patients in whom Dionosil Oily was used. The low surface tension characteristic of this aqueous, yet viscous, solution resulted in excellent and uniform coating of the bronchial mucosa. The radiographic contrast and density was at least equal to that obtained with the use of iodized bronchographic contrast materials. The elimination of barium sulfate was rapid except in 3 (of 50) patients who had severe emphysema. There was no experimental or clinical evidence of chronic fibrosis or foreign-body granulomata resulting from the use of barium or sodium carboxymethylcellulose. While the retention of barium sulfate is almost certainly no more likely than the retention of any other contrast medium, it would probably be wise to avoid its use for bronchography in patients who have severe pulmonary emphysema.

Although our animal histopathologic data and subsequent clinical work failed to show any undesirable chronic pulmonary changes following the use of a proprietary mixture of barium (Micropaque) suspended in saline containing 1.5 per cent carboxymethylcellulose, we nevertheless believe it is desirable to use nonproprietary barium mixtures of known composition. We are now studying mixtures of nonproprietary chemically pure barium sulfate and various suspending agents. We believe, also, that it is advisable to use saline containing 2 or 3 per cent sodium carboxymethylcellulose in preparing the barium mixture in order to increase its viscosity, and thereby fur-

ther diminish the possibility of alveolization.

Bismuth subcarbonate suspensions are not considered safe bronchographic media, since histopathologic studies of animal lungs showed severe changes as long as ten weeks following injection into the tracheobronchial tree.

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SUMMARIO IN INTERLINGUA

Suspensiones de Sulfato de Barium e de Subcarbonato de Bismuth Como Substantias de Contrasto in le Bronchographia

Experimentos in conilios e essayos clinic in humanos monstra que sulfato de barium (Micropaque) suspendite in normal solution salin, con un contento de al minus 1,5 pro cento de carboxymethylcellulosa a sodium como augmentator del viscositate, es un salve e efficace substantia de contrasto pro objectivos bronchographic.

In le experimentos animal, sulfato de barium, subcarbonato de bismuth, Dionosil Oily, e Lipiodol esseva administrate per via transtracheal, e le replenation del bronchos de lobo inferior e le elimination del substantia esseva observate per roentgenogrammas serial. Le responsa histopathologic a omne le substantias esseva predominantemente un reaction a corpore alien. Le alterationes que occurreva post administrationes de subcarbonato de bismuth esseva ancora obvie post un intervallo

de dece septimanas. Per consequente, iste substantia esseva rejicite. Nulle effectos permanente esseva observate post administrationes del altere substantias, e al fin de dece septimanas, nulle signo esseva notate de residuos de illos in le alveolos.

In subjectos human, studios comparative esseva facile con Dionosil Oily (considerate como le melior del disponibile substantias de contrasto a contento de iodo) e con sulfato de barium. Bronchographia a sulfato de barium esseva sequite per un plus basse incidentia de elevation de temperatura e de acceleration del pulso que Dionosil Oily, e le contrasto radiographic effectuate per sulfato de barium esseva al minus equal a illo effectuate per preparatos a contento de iodo. Post le uso del substantia a barium nulle signo de fibrosis chronic o de granulomas a corpore alien esseva constatare.



An Evaluation of Orabilex (Bunamiodyl), a New Medium for Cholecystography¹

ABRAHAM GEFFEN, M.D.

THE REMARKABLE progress which has been made in the development of contrast media for oral cholecystography has led from time to time to the belief that the ideal medium has been found (1). More complete reports, however, have revealed certain disadvantages and limitations in all oral media currently employed. Of particular significance in this respect is occasional unexplained nonvisualization with a single dose of contrast material, necessitating a repeat examination with increased dosage. Other factors to be taken into consideration are the obscuring of disease by intestinal residue and the occurrence of gastrointestinal and urologic side-effects.

The contrast medium of choice should provide maximum safety and patient tolerance with a minimum of side-effects, effective and dependable visualization of the gallbladder, and freedom from secondary shadows due to retention in the intestinal tract. In studies in France, where it was first introduced, Orabilex (Bunamiodyl), a triiodinated compound—3(3-butyrylamino-2,4-6-triiodophenyl)-2 ethyl sodium acrylate—containing 57 per cent iodine by weight appeared to meet these criteria (2). The iodine content of iopanoic acid, or Telepaque, is 66.7 per cent by weight.

Absorption: Orabilex is absorbed readily from the small intestine, selectively excreted in the bile, and concentrated in the gallbladder. Optimal density of opacification of the gallbladder is obtained in thirteen to sixteen hours. The butyrylation of the amine group is considered to permit adequate dosage essential for best results, with the incidence of side-effects considerably less than has been reported with other triiodinated compounds.

Excretion: Orabilex is excreted largely through the kidney, without the attendant dysuria observed with similarly excreted agents. As a consequence, there is a much lower incidence of intestinal residue and the cholecystogram is unobscured.

Toxicity: In acute intravenous toxicity studies in mice, the LD 50 value for Orabilex was found to be 570 mg. per kilogram as compared to 360 mg. per kilogram for iopanoic acid and 400 mg. per kilogram for iodoaliphonic acid (3).

When 200 mg. per kilogram, in the form of a 5.4 per cent solution, is administered to cats by means of a stomach tube, the animals show no signs of discomfort. Nor do rabbits exhibit any side-reactions when 200 mg. per kilogram in the form of a 5 per cent solution is introduced into the marginal vein of the ear. Dogs receiving Orabilex in doses up to 1.5 gm./kg. showed no impairment of liver or kidney function and, when the animals were sacrificed, gross and microscopic studies revealed no organ damage (4).

Contraindications: As is the case with other cholecystographic media, Orabilex is contraindicated in patients with acute nephritis and uremia. It should not be administered in the presence of disorders of the gastrointestinal tract which might prevent its absorption.

MATERIAL AND METHODS

Recently, Orabilex was made available to us for clinical study. It was administered orally to 78 patients in an effort to evaluate its merits. Of the 78 patients, 67 were females, reflecting the sex distribution generally associated with suspected biliary tract disease. Thirty-one patients were sixty years of age or older. The next largest group in point of age was that from

¹ From the Department of Radiology, Beth Israel Hospital, New York, N. Y. This study was made possible by E. Fougera & Co., Inc., who supplied the Orabilex used. Accepted for publication in September 1958.

TABLE I: VISUALIZATION WITH ORABILEX

	6.0 gm. Orabilex	4.5 gm. Orabilex	Total
No of patients	30	48	78
Nonvisualization*	1	8	9 (12%)
Visualization	29	40	69 (88%)
Excellent (4+)	18 (62%)	27 (68%)	45 (65%)
Good (3+)	6 (21%)	11 (27%)	17 (25%)
Fair (2+)			
Faint or poor (1+)	5 (17%)	2 (5%)	7 (10%)

* In none of the cases with nonvisualization was visualization achieved on a repeat examination with iopanoic acid.

thirty to thirty-nine years, numbering 16. Weight was not a determinant in selection either of patient or dosage.

On the basis of dosage, the patients were divided into two groups. Each of the first 30 was given 6 gm. (six tablets of 1.0 gm. each). In the second group, consisting of 48 patients, the dose was 4.5 gm. in the form of tablets or capsules of 0.75 gm. each.

Technic of Examination: A preliminary film of the right upper abdomen was obtained and, on the day prior to x-ray examination, the patient was allowed a regular diet for lunch but was given (or instructed to have) a low-fat or no-fat supper at 6 P.M. Beginning at 7 P.M., the 6 tablets or capsules were swallowed one at a time, at five-minute intervals, with small amounts of water. The patient was allowed nothing else by mouth until completion of the examination at nine o'clock the following morning.

Films were taken in the postero-anterior and left oblique prone positions and were immediately processed and viewed. When indicated, additional views were obtained. If the gallbladder was visualized satisfactorily, a fatty meal, consisting of an eggnog (the yolks of two eggs and 2 ounces of cream) was given. Ten minutes later, a supine oblique view was obtained (Shehadi, 5) for visualization of the ducts, and at thirty minutes a prone oblique view for the same purpose. If small stones were noted, especially in a patient recovering from a recent episode of biliary colic, the fatty meal was not given.

To verify the radiographic reliability of the new medium, if the gallbladder was

visualized only faintly or not at all, iopanoic acid (3.0 gm.) was administered the same day and filming was repeated the next day. This was followed in most instances by intravenous cholangiography.

Painstaking radiographic technic is essential for good oral cholecystography. The technical factors uniformly used were: 300 ma, 0.2-0.4 seconds, and 70-80 kv, with small cone.

CLINICAL OBSERVATIONS AND EVALUATION

1. *Degree of Visualization:* Visualization was achieved in 69 patients; in only 9 was it completely absent. The results with 6.0- and 4.5-gm. doses were not significantly different, indicating that the latter dosage is as effective as the larger one. The relative frequency of the degree of visualization is set forth in Table I.

2. *Presence of Calculi:* Twenty patients (29 per cent) of those with visualized gallbladders had stones, and 1 a papilloma. Both radiolucent and radiopaque calculi were delineated, the radiolucent type being found in 11 cases, and the radiopaque in 10 (1 patient had both kinds). A calculus was present in only 1 of the 9 nonvisualized gallbladders.

3. *Response to Fatty Meal:* Satisfactory contractility was observed in 63 per cent of the 60 patients who were given a fatty meal. Orabilex did not appear to interfere with physiological contraction or emptying of the gallbladder.

4. *Duct Visualization:* Visualization of the cystic or common duct was excellent or good in 40 per cent of the patients (Column 1, Table II) and faint in an additional 23 per cent.

5. *Residue:* There was minimal or moderate colonic residue, primarily of a diffuse, non-discrete nature, in 33 per cent of those receiving 6.0 gm. Of those who had been given the 4.5-gm. dose of Orabilex only 19 per cent had any residue, and in all except 1 this was minimal. In none did it interfere with visualization.

6. *Side-Effects:* Eighty per cent of the 78 patients receiving Orabilex showed no

TABLE II: COMPARISON OF ORABILEX WITH OTHER MEDIA (FINDINGS FROM SIX INVESTIGATIONS)

	Geffen (Orabilex)	Shehadi (5) Telepaque (Iopanoic Acid)	Reynolds and Fulton (1) Telepaque (Iopanoic Acid)	Whitehouse and Martin (6) Telepaque (Iopanoic Acid)	Whitehouse Teridax (7) (Iophenoxic Acid)	Dunne <i>et al.</i> (8) Telepaque (Iopanoic Acid)	Root and Lewis (9) Teridax (Iophenoxic Acid)
Dosage (gm.)	4.5-6.0	3.0-6.0	2.0-8.0	3.0	3.0	2.0-2.5	3.0-6.0
No. cases	78	310	1,000	500	155	426	472
Degree of visualization*							
Excellent (4+)	65%	37%	28%	66%	12%	10%	49%
Good (3+) and fair (2+)	25%	58%	65%	26%	54%	89%	44%
Poor or faint (1+)	10%	5%	7%	8%	34%	1%	7%
Nonvisualization†	12%	18%	9%	11%	21%	3%	8%
Visualization of bile ducts (good to ex- cellent)	40%	50%	58%	‡	‡	‡	‡
Intestinal residue	19% (with 4.5 gm.) 33% (with 6.0 gm.)	‡ ‡	‡	97%‡	8%	‡	3.4%
Side-effects							
None	80%	‡	‡	63%	71%	‡	‡
Nausea	9%	10%	‡	6%	14%	1.9%	13%
Vomiting	1%	0.3%	‡	0.5%	2%	0	0.9%
Diarrhea	0	15%	‡	25%	10%	8.8%	16.6%
Dysuria	0	6%	‡	14%	10%	8.2%	11%

*Data corrected so as to give percentages as on total number of cases visualized.

† Repeat examination with iopanoic acid unsuccessful in all nonvisualized cases.

‡ Percentages not reported.

side-effects. This is one of the most significant findings in the study and represents an important advance in cholecystographic media. Side-effects occurred in 16 cases but in only 5 were these severe, as evaluated subjectively by the patient. In addition to those enumerated in Table II, epigastric pain was a complaint of 5 patients and heartburn of 1. Two patients reported transitory cramps and there was 1 mild skin eruption. Because certain side-effects, such as epigastric pain, were often part of the presenting symptomatology, their enumeration as untoward effects is in doubt. They are included solely for the sake of completeness.

7. *Analysis of the Nonvisualized Gallbladders:* In 8 of the 9 cases in which the gallbladder was not visualized with Orabilex, repeat examinations the following day with 3.0 gm. of iopanoic acid were also unsuccessful. Intravenous cholangiography was then performed in 7 of the 9. In 3 of these cases the gallbladder was visualized and all 3 showed the presence

of calculi. Disease was thus demonstrated in all the gallbladders which Orabilex had failed to visualize.

COMPARISON OF ORABILEX WITH OTHER ORAL MEDIA

To initiate a control series for comparative analysis would have duplicated previous excellent studies (1, 5-10). The results of these earlier investigations have, therefore, been summarized in Table II for comparison with the findings obtained in the present study.

1. *Degree of Visualization:* In order to compare the degree of visualization, it is necessary first to be certain that the data in all the studies are comparable. Since the number of gallbladders visualized will vary with the composition of the particular group selected for study, the degree of visualization, if expressed as a percentage of the total number of patients, will not truly represent the efficacy of the medium employed (e. g., a survey type of study of largely well patients may give quite dif-

ferent results from a series including many patients with gallbladder disease). In their study with iopanoic acid, Reynolds and Fulton (1) tabulated the degree of opacification as a percentage of the total number of cases visualized. This method of computation for each degree of visualization has been followed in this study (Column 1, Table II). Shehadi (5), Whitehouse and Martin (6), Whitehouse (7), Dunne *et al.* (8), and Root and Lewis (9) in their reports included the nonvisualized cases in the totals for determining percentages. I have corrected the data from their original articles to represent percentages of only those visualized.

In degree of visualization achieved, either dose of Orabilex (4.5 or 6 gm.) is equal to 3.0 gm. of iopanoic acid, better than 3.0-6.0 gm. of iophenoxic acid, and much to be preferred to 2.0 to 2.5 gm. of iopanoic acid.

2. *Visualization of Bile Ducts:* Orabilex gives good or excellent visualization of the bile ducts in 40 per cent of the cases, somewhat less than the totals reported for iopanoic acid; however, the latter figures have not always been classified as to excellence of visualization.

3. *Residue:* With Orabilex the incidence of intestinal residue is markedly lower than has been reported with iopanoic acid but slightly greater than with iophenoxic acid.

4. *Side-Effects:* With 80 per cent of the patients showing no side-effects at all, Orabilex appears to represent a significant improvement over iopanoic acid (no side-effects in 63 per cent) and iophenoxic acid (no side effects in 71 per cent). It is most significant that in this series with Orabilex there was no incidence of diarrhea or dysuria, these troublesome side-effects occurring fairly frequently with the other two media.

SUMMARY AND CONCLUSIONS

Orabilex, a new cholecystographic medium, has been given to 78 patients, and the results have been compared to

those reported for Teridax (iophenoxic acid) and Telepaque (iopanoic acid).

Orabilex appears to be safe, effective, and valuable for visualization of the gallbladder. A 4.5-gm. dose appears to be fully as effective as the 6.0-gm. dose.

In all cases of nonvisualization with Orabilex, the reliability of this finding as a diagnostic sign of gallbladder disease has been confirmed by follow-up studies.

Orabilex, 4.5 gm., gives visualization comparable to iopanoic acid, 3.0 gm., with a notably lower incidence of side-effects. On both scores (visualization and side-effects) Orabilex is superior to iophenoxic acid.

ADDENDUM

Since submission of this article, Orabilex was given to an additional 22 patients, making a total of 100 in this series. The same favorable results as to visualization, side-effects, and residue were obtained. If duct visualization is based on percentage of those given fatty meals, excellent or good duct visualization was obtained in 53 per cent, which compares favorably with the best figures for Telepaque.

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SUMMARIO IN INTERLINGUA

Un Evaluatión de Orabilex (Bunamiodyl), un Nove Substantia de Contrasto pro le Cholecystographia

Orabilex, un nove substantia de contrasto pro le cholecystographia, eseva administrate a 78 patientes, e le resultatos eseva comparate con illos reportate pro Teridax (acido iophenoxic) e pro Telepaque (acido iopanoic).

Orabilex pare esser salve, efficace, e utile in le visualisation del vesica biliari. Un dose de 4,5 g es apparentemente non minus efficace del toto que un dose de 6,0 g.

In omne casos de non-visualisation con

Orabilex, le valor positive de iste constatacion como signo diagnostic de morbo del vesica biliari eseva confirmate per studios consecutori.

Orabilex, in doses de 4,5 g, effectua un visualisation comparabile a illo effectuate per acido iopanoic in doses de 3,0 g, sed le incidentia de effectos lateral es notabilmente plus basse. In ambe respectos—visualisation e effectos lateral—Orabilex es superior a acido iophenoxic.



Hydronephrosis Following Retrograde Pyelography¹

JOHN W. HOPE, M.D., and ALEXANDER J. MICHIE, M.D.²

"THE PELVOCALYCEAL collecting systems are poorly visualized; advise a retrograde pyelogram." This is a common recommendation following intravenous urography in many departments of radiology.

Prior to the present study, the authors, using the renal clearance technic, had found that ureteral catheterization disturbed kidney function (1). In unilateral catheterization a greater volume of urine is formed by the catheterized kidney, but solute excretion by the two kidneys is essentially equal. When a wire stylet is required for insertion of the catheter, this difference in simultaneously formed urine by the two kidneys is exaggerated. Accordingly, ureteral trauma provokes an increase in water excretion: the greater the trauma, the larger the volume of water excreted. It occurred to us that these physiological observations might be reproduced more graphically with radiological studies.

METHOD OF STUDY

With the above problem in mind, the authors selected 14 children for intravenous urography, to be followed by retrograde pyelography and finally by repeat intravenous urography within sixteen hours of the retrograde study (Table I). All had either a urinary tract infection or hematuria. The studies were carried out in 1953, when, for the most part, 35 per cent Diodrast was the contrast medium employed.

RESULTS

In 9 of the 14 children studied, the second urogram showed ureteral abnormalities not previously present: the changes were severe in 1, moderate in 4, and mini-

mal in 4. In 5 children no change was demonstrable after the retrograde pyelogram (Table I).

The 3 illustrative case reports which follow demonstrate what is meant by severe and moderate.

CASE REPORTS

CASE I: A. S., a 3-year-old girl, had a normal urogram on Jan. 14, 1953 (Fig. 1, A). Except for overfilling on the left, the retrograde pyelogram two days later was also normal (Fig. 1, B). The repeat urograms on Jan. 17 (Figs. 1, C-E) show severe impairment of renal function, with only a nephrogram showing up at fifteen minutes and dilatation of the pelvocalyceal collecting systems at one and two hours. It is of interest that it was on the left side that overdistention took place on the retrograde study; yet it is the right kidney in which function is most seriously impaired. The significant observation on retrograde pyelography was that the catheters could not be inserted beyond the lower third of each ureter, and considerable difficulty was encountered in passing them even to this height.

CASE II: J. N., a 6-year-old girl, had a normal urogram on Jan. 13, 1953 (Fig. 2, A) and, except for slight overfilling, a normal retrograde pyelogram the next day (Fig. 2, B) with the catheters in the upper pole of each kidney. The repeat urogram on Jan. 15 shows the right upper urinary tract to be unaffected by the ureteral catheterization, but on the left there is moderate dilatation of the entire urinary drainage tract (Fig. 2, C and D). These changes were temporary, a urogram on Nov. 6, 1956, again showing no abnormality (Fig. 2, E).

CASE III: M. M., a 12-year-old girl, had a normal urogram on July 22, 1953 (Fig. 3, A). Only the thirty-minute film is shown here for comparison with the second study. All of the contrast medium has already cleared the left side and only a faint shadow persists on the right. The bladder is full of the opaque material. A normal retrograde pyelogram was obtained on the afternoon of the same day (Fig. 3, B). The catheters are seen to be in the lower third of each ureter. Considerable difficulty was encountered in passing them even to this height. The repeat urogram on July 23 shows ineffectual trans-

¹ From the Departments of Radiology and Surgery, The Children's Hospital of Philadelphia. Accepted for Publication in September 1958.

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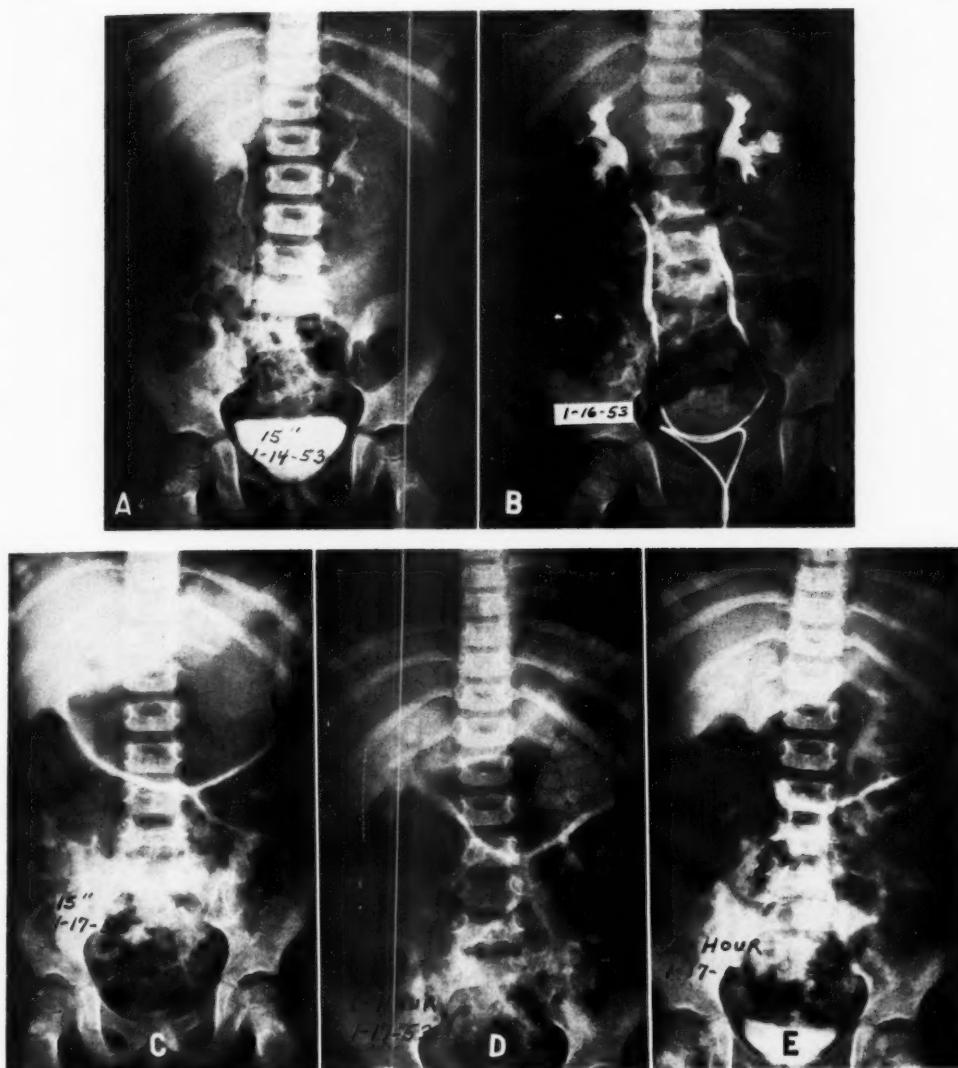


Fig. 1. Case I. A. S., a 3-year-old girl studied because of frequency and urgency.

- A. Intravenous urography, Jan. 14, 1953: fifteen-minute film, normal.
- B. Retrograde pyelography, Jan. 16: a normal study except for some overfilling on the left side.
- C. Repeat intravenous urography, Jan. 17: fifteen-minute film, showing a faint nephrogram on each side.
- D. Repeat intravenous urography, Jan. 17: one-hour film showing poor function and dilatation of each pelvocalyceal collecting system.
- E. Repeat intravenous urography, Jan. 17: two-hour film showing the prolonged excretion of the contrast medium.

port of the contrast agent from both kidneys and moderate dilatation of each pelvocalyceal collecting system (Fig. 3, C). The post-voiding one-hour film shows an obstruction at each ureterovesical junction (Fig. 3, D), and the extent of this functional impairment is seen in the two-hour film (Fig. 3, E).

DISCUSSION

It is obvious from this study that ureteral catheterization is not a totally innocuous procedure. The degree of renal impairment is probably secondary to trau-

TABLE I: OBSERVATIONS ON FOURTEEN CHILDREN FOLLOWING RETROGRADE PYELOGRAPHY

Patient	Sex and Age	Symptoms	First Intravenous Urogram	Retrograde Pyelogram	Second Intravenous Urogram
1. A. S. Case I	F 3 yr.	Frequency and urgency	20 c.c. 35% Diodrast Normal study	Catheters: In lower third of ureters; overfilling on left side Normal study	Severe dilatation of each kidney and delayed appearance of contrast medium
2. J. N. Case II	F 6 yr.	Hematuria	20 c.c. 35% Diodrast Normal study	Catheters: In pelvis; slight overfilling on each side Normal study	Moderate stasis of left ureter with dilatation of left pelvocalyceal system; normal on right
3. M. M. Case III	F 12 yr.	Pyuria and flank pain	20 c.c. 70% Urokon Normal study	Catheters: In lower third of ureters Normal study	Moderate stasis of each ureter down to ureterovesical junction
4. E. T.	M 9 yr.	Hematuria	40 c.c. 35% Diodrast Normal study	Catheters: Right in pelvis; left in upper third of ureter Normal study	Moderate stasis of right kidney and ureter down to upper third of ureter; normal on left
5. P. M.	F 4 yr.	Dysuria, frequency, and pyuria	20 c.c. 35% Diodrast Normal study	Catheters: In pelvis Normal study	Moderate stasis of each ureter down to ureterovesical junction
6. P. F.	F 8 yr.	Hematuria	25 c.c. 70% Urokon Normal study	Catheters: Right in upper pole; left in midpelvis; slight overfilling on right Normal study	Minimal stasis of right ureter; kidneys unchanged
7. W. K.	M 12 yr.	Hematuria	20 c.c. 35% Diodrast Normal study	Catheters: In midureters Normal study	Minimal stasis of left ureter; kidneys unchanged
8. S. S.	F 5 yr.	Fever, pyuria, and hematuria	20 c.c. 70% Urokon Bilateral irritable kidneys	Catheters: Right in upper pole; left in pelvis Normal study	Minimal stasis of each ureter
9. J. W.	F 9 yr.	Recurrent fever, pyuria, and hematuria	20 c.c. 70% Urokon Normal study	Catheters: Right in pelvis; left in upper pole Normal study	Minimal stasis of each ureter
10. W. G.	M 6 yr.	Hematuria	20 c.c. 35% Diodrast Normal study	Catheters: Right in midureter; left in upper third of ureter Normal study	No change
11. M. F.	M 4 yr.	Hematuria	20 c.c. 35% Diodrast Minimal clubbing of right upper calyx and irritable left pelvocalyceal collecting system	Catheters: Right in pelvis; left in midureter Normal study	No change
12. V. B.	M 5 yr.	Hematuria	25 c.c. 70% Urokon Normal study	Catheters: In pelvis Normal study	No change
13. T. H.	M 5 yr.	Fever, pyuria, and hematuria	20 c.c. 70% Urokon Clubbing of calyces on right and dilatation of urethra due to metal stricture	Catheters: Right in midureter; left at ureteropelvic junction Normal study	No change
14. L. L.	F 10 yr.	Recurrent pyelonephritis	20 c.c. 35% Diodrast Bilateral clubbing of calyces	Catheters: In upper third of ureters Normal study	No change

ma which causes edema of the ureteral mucosa. This, in turn, produces partial obstruction to urinary flow. Because of the smaller diameter of the urethra and ureters in children, one would expect greater

impairment in this age group. It has been shown that the changes are transient (Case II), but urinary stasis of any degree predisposes to infection and should be avoided. In this hospital it has been

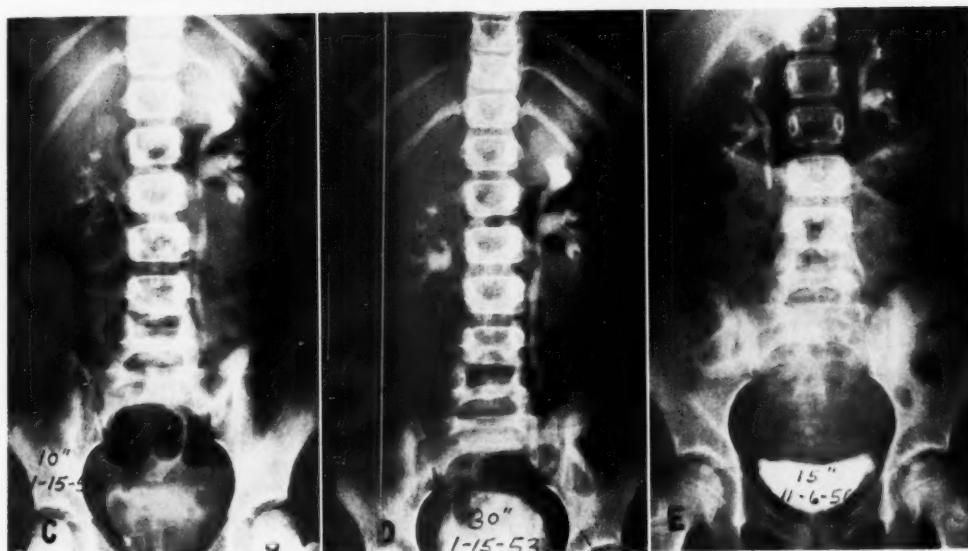
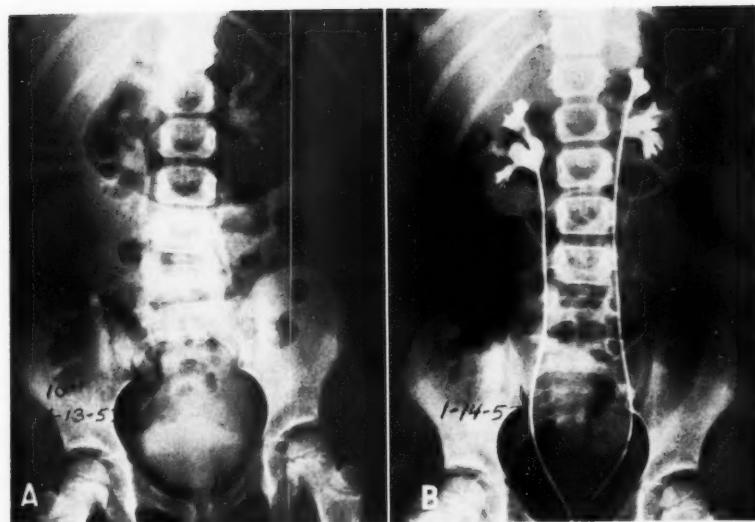


Fig. 2. Case II. J. N., a 6-year-old girl studied because of hematuria.

- A. Intravenous urography, Jan. 13, 1953: ten-minute film, normal.
- B. Retrograde pyelography, Jan. 14: Normal except for slight overfilling on each side.
- C. Repeat intravenous urography, Jan. 15: ten-minute film showing the right side to be normal, while on the left side there is moderate dilatation of the entire urinary drainage tract.
- D. Repeat intravenous urography, Jan. 15: thirty-minute film showing prolonged excretion on the abnormal left side.
- E. Intravenous urography, Nov. 6, 1956: fifteen-minute film showing a return to normal. Comparable to the original study.

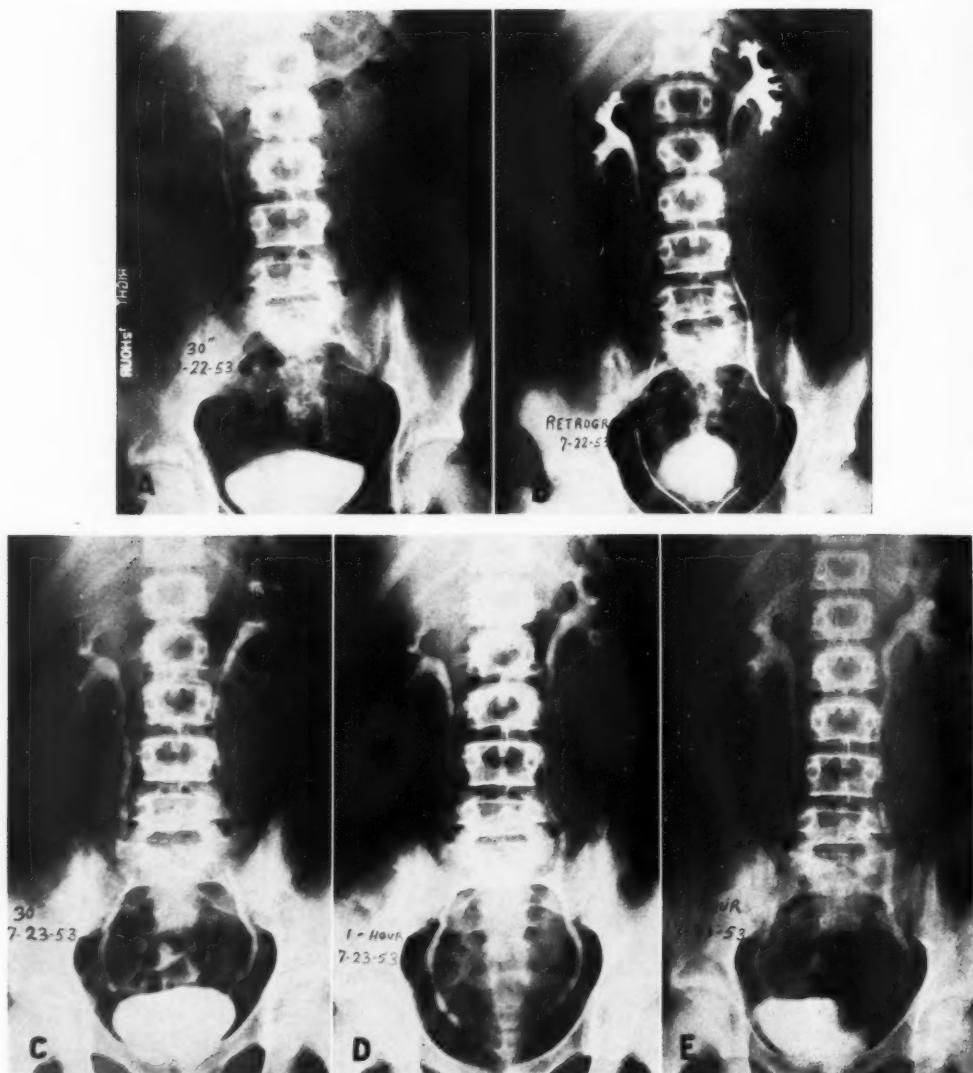


Fig. 3. Case III. M. M., a 12-year-old girl studied because of pyuria and flank pain.

A. Intravenous urography, July 22, 1953: thirty-minute film. All of the contrast medium has cleared the left side, and only a faint shadow of opaque material remains on the right. The thirty-minute film was chosen for comparison with the repeat study.

B. Retrograde pyelogram made on same day as the initial urogram, normal.

C. Repeat intravenous urography, July 23: thirty-minute film showing moderate dilatation of each pelvocalyceal collecting system and abnormally dilated ureters in comparison with original study.

D. Repeat intravenous urography, July 23: Post-voiding one-hour film showing an obstruction of each ureter at the ureterovesical junction.

E. Repeat intravenous urography, July 23: two-hour film showing that rather severe obstruction still persists.

possible to eliminate almost entirely the necessity for retrograde pyelograms by perfecting the technic of intravenous urography (2, 3).

Accordingly, we rarely advise a retrograde pyelogram.

SUMMARY

1. Nine of 14 children studied by means of intravenous urography showed some degree of impaired renal function following retrograde pyelography.

2. Ureteral catheterization is not a totally innocuous procedure.

3. Intravenous urography is preferable to retrograde pyelography, and every effort should be made to arrive at a diagnosis without resorting to ureteral catheterization.

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SUMMARIO IN INTERLINGUA

Hydronephrosis post Pyelographia Retrograde

Catheterismo ureteral, specialmente in pacientes pediatric, non es un processo completamente innocue. Novem ex 14 juveniles studiate per medio de urographia intravenose monstrava un certe grado de compromisso del function renal post pyelographia retrograde. Presumitemente, le damno esseva secundari a trauma. Le trauma causava edema del mucosa ure-

teral, e isto de su parte produceva un obstruction partial del fluxo de urina. Iste alterationes es transitori, sed omne grado de stase urinari predispone a infectiones e debe esser evitate.

Urographia intravenose es preferibile a pyelographia retrograde, e omne effortio debe esser facite pro arrivar al diagnose sin recurso a catheterismo ureteral.



The "Ponticulus Posticus" of the First Cervical Vertebra¹

JOHN PYO, M.D., and ROBERT M. LOWMAN, M.D.

THE EVALUATION of anatomic landmarks is an important task of the radiologist because significant changes in these structures may be an index to underlying disease processes. The variations and asymmetrical deviations of such landmarks in size, shape, and contour are often many and confusing. For this reason they must be studied with care to insure adequate differentiation from disease processes.

called the vertebral artery sulcus (Fig. 1). This sulcus, situated on the posterolateral margin of the posterior arch of the atlas varies in size and in some instances is very deep. To the posterior arch of the atlas is attached, inferiorly and posteriorly, the posterior occipital ligament, which is connected above with the posterior margin of the foramen magnum. This ligament is a broad but thin membranous sheet in-

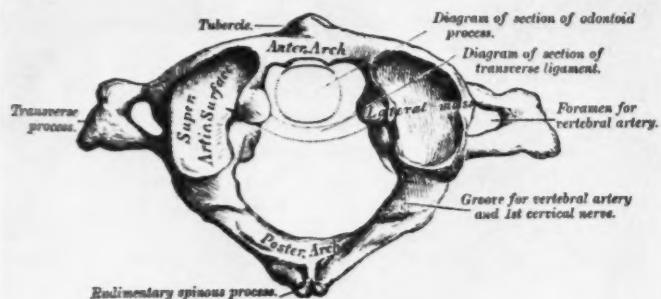


Fig. 1. The 1st cervical vertebra as seen from above, showing the groove formed by the vertebral artery. The artery ascends in the foramen in the transverse process of the vertebra, then follows a posterior and mesial course, crossing the vertebral arch in the groove and entering the foramen magnum. (From Gray's Anatomy.)

The extensive variations which may occur in the region of the craniocervical junction have been reviewed by McRae (6). Hoare (3) has also pointed out the importance of evaluating the grooves and foramina in the region of the posterior and lateral margins of the atlas and axis in vascular lesions of the posterior fossa and in lesions involving the cerebellum. It appeared desirable to us to evaluate the sulcus formed by the vertebral artery as it crosses the posterolateral laminar margin of the first cervical vertebra.

After its exit from the transverse foramen, the vertebral artery passes over the posterior arch of the atlas, forming a groove

timately blending with the dura. Its lateral divisions are known as the oblique atlanto-occipital ligaments. These ligaments are incomplete at their inferior margins, affording with the vertebral artery sulcus an opening for the passage of the vertebral artery and suboccipital nerve (Fig. 2). At times an anomalous ossification center occurs in the ligament, and bridges the sulcus. This bony arch—the ponticulus posticus—encloses the foramen arcuale or posterior atlantoid foramen, and through this the suboccipital nerve and vertebral artery pass as they course over the upper surface of the first vertebra.

The ponticulus has been described as

¹ From the Department of Radiology, The Memorial Unit, Grace-New Haven Community Hospital, and Yale Medical Center, New Haven, Conn. Accepted for publication in August 1958.

Kimmerle's anomaly (4, 5). As late as 1955 one American text on the spine erroneously designated the structure as the foramen transversarium (1). Writers in general do not evaluate its variations in size, its occurrence in the general population, or its sex incidence. Our interest in

The males showed a range from newborn to ninety years, with an average of 48.9 and a median of fifty-seven years.

Thirty-eight (12.6 per cent) of the skulls examined showed a ponticulus. Twenty of these (6.6 per cent of the 300) were in females, with an age range from seventeen

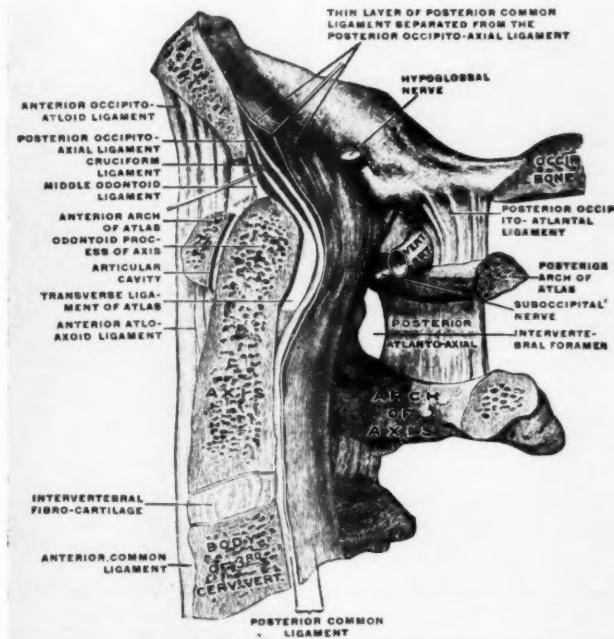


Fig. 2. A median section through the occipital bone and the upper three cervical vertebrae with the ligaments in position. The passage of the vertebral artery and the suboccipital nerve over the posterior arch of the atlas is shown here. The ossification in the margins of the posterior occipito-atlanto ligament produces the ponticulus. (From Gray's Anatomy.)

this anatomic structure was stimulated by its incidental demonstration in various skull examinations. We therefore undertook a review of the roentgenograms of 300 normal skulls, taken for the most part from routine studies or examinations for possible metastases, which had proved negative. Cases with definite evidence of intracranial or calvarial lesions were excluded.

Of the 300 patients represented, 170 (56.6 per cent) were females and 130 males. The females ranged in age from newborn to eighty-seven years, the average being fifty-two and the median forty-nine years.

to seventy-six years, with an average of 47.1 and a median age of fifty years. For the 18 male cases the age ranged from ten to seventy-five years with average and median ages of 52.6 and sixty years, respectively. The sex incidence of the ponticulus is thus, for all practical purposes, approximately equal, 6.6 and 6.0 per cent.

Not all the ponticuli in this series were bilateral; 12 (31.6 per cent of the 38 cases; 4 per cent of the 300 skulls) were unilateral. The sex distribution of these 12 cases was equal. It was difficult to determine on which side the anomaly occurred more fre-



Fig. 3. Lateral film showing the arcuate calcification bridging the vertebral groove. The bridge arches backward from the posterior extremity of the superior articular process and forms the ponticulus posticus. The foramen arcuale is enclosed beneath the margins of the ponticulus. The bridging in this case is bilateral.

quently, since in many cases only a single lateral skull film was available. In some instances complete arching was demonstrated; in others fusion was incomplete (Figs. 3 and 4). The 26 bilateral ponticuli constituted 8.6 per cent of the total number of skulls studied.

There were numerous variations in respect to size, configuration, and position of the ponticuli due to differing radiographic projections (Fig. 5, A). In some cases of ossifications developing in the oblique atlanto-occipital ligaments the arcuate bridging was incomplete and difficult to recognize; in others it was thick and of an amorphous character; in still others there appeared to be intimate fusion with the posterior margins of the superior articular processes, with bony trabeculae extending into the arc of the ponticulus. When ossification was incomplete, the defect was usually found at the posterior margin (Fig. 6). Incomplete ossification, however, may be found at any point in the arch. The sulcus for the passage of the vertebral artery also varied widely. Sometimes the laminar margins showed little or no depression; in other cases, the superior margin of the lamina of the first cervical vertebra was thick, and a deep U-shaped sulcus was present. Some of the ponticuli were obscured by the pneumatization of

the mastoid and the position of the occiput. In one case the presence of a ponticulus was simulated by an overlying mastoid (Fig. 5, B).

Both Hadley (2) and Pendergrass (7) have pointed out that the ponticulus posticus represents a structure without clinical significance, arising from the ossifi-



Fig. 4. Unilateral bridging of the ponticulus. Note the thinning of the posterior margins of the ponticulus and the posterior arch of the atlas.

cation of the posterior portion of the atlanto-occipital ligament and commonly seen in lateral projections of the cervical spine. Other authors, however, believe that, just as an enlargement of the carotid canal indicates hypertrophy of the carotid artery in cases of large supratentorial venous aneurysm, so changes in the bony canal through which the vertebral arteries pass indicate enlargement of these arteries. Thinning and enlargement of these grooves have been found with vascular lesions occurring in the posterior fossa of the skull (3).

Grooves in the posterior arch of the atlas can be adequately seen in the lateral films of the skull and enlargements of these foramina may be detected in such views. To determine the normal variations of size, the ponticuli postici were measured directly on the radiographs. The average size was 8.5 mm. Among the females the range was from 6 to 11 mm., the average being 8.3 mm. and the median 8 mm. Among males the range was from 6 to 12 mm., the average 8.7 mm. and the median 8.5.

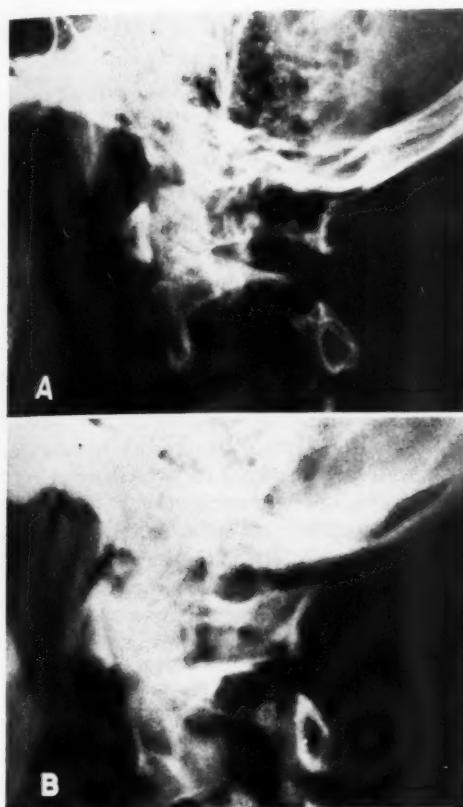


Fig. 5. A. Changes in the appearance of bilateral ponticuli produced by oblique positioning of the head. B. Pneumatized mastoid air cells producing an appearance which simulates a ponticulus.

CONCLUSION

It must be inferred from reports by other investigators that widening of the grooves and foramina of the first cervical vertebra aid in the diagnosis of lesions in areas supplied by the vertebral arteries. Our study of 300 skulls, however, has indicated that a wide range of anatomic variation in the shape, size, and contour of the ponticulus may occur. In addition, the study has shown that complete or partial bridging of the arcuate rim occurs in approximately 12 or 13 per cent of the population, principally in the age group beyond forty. Thus, minimal or moderate changes produced by an enlarged vertebral artery may be difficult to recognize.

It has been the aim of this report to

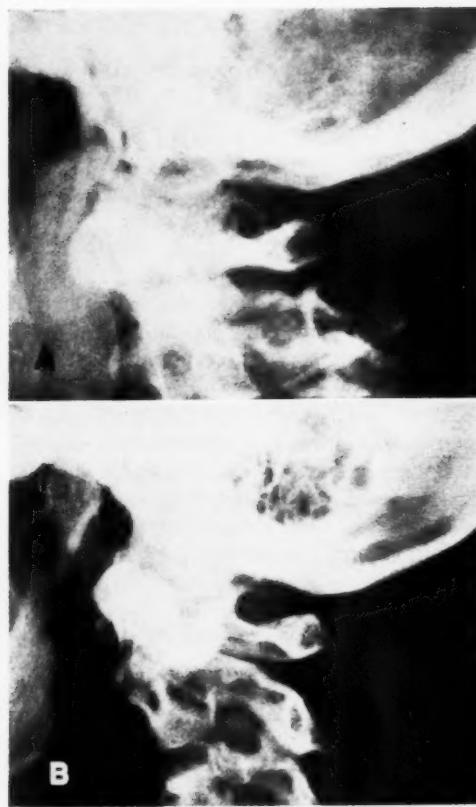


Fig. 6. A. Complete formation of a ponticulus on one side, with incomplete ossification on the other.

B. Incomplete ossification of the ponticulus bilaterally.

describe the occurrence, the variable character, and appearance of the ponticulus. Further study is indicated to evaluate the use of this anatomic landmark as a clue in the radiologic diagnosis of lesions in the posterior fossa and the upper cervical cord.

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SUMMARIO IN INTERLINGUA

Le Ponticolo Postic Del Prime Vertebra Cervical

Le ponticolo postic es un anomale centro de ossification que es formate in le portion oblique del ligamento atlanto-occipital e que ponta le sulco del arteria vertebral. In un effortio de evalutar le dimensiones, apparentia, e frequentia de iste structura, le roentgenogrammas de 300 cranios normal esseva examine. Un ponticolo esseva discoperte in 38 casos (12,6 pro cento). Le anomalia occurreva principalmente in patientes post le etate de 40 annos e in distribution equal inter le sexos.

Roentgenographicamente le apparentia del ponticolo e del sulco pro le passage de

arteria vertebral monstrava multe variationes. Le pontamento se monstrava unilateral o bilateral, complete o incomplete. Le grandor medie del structura esseva 8,5 mm con valores minimo-maximal de 6 e 12 mm. In vista de iste observationes, alterationes minime o moderate producute per un allargate arteria vertebral pote esser difficile a recognoscere.

Studies additional es indicate pro evaluar le signification de iste punto de referentia anatomic como indicio in le diagnose radiologic de lesions in le fossa posterior e in le chorda cervical superior.



Experimental Results with the Panel X-Ray Amplifier¹

B. KAZAN, M.A.,² and E. W. GODFREY, M.D.³

DURING THE PAST decade, the field of solid-state physics has expanded greatly. One aspect of this growth is the advance made in the field of electroluminescent phosphors. With these materials it is possible to produce a pattern of emitted light from a flat sheet by direct application of voltages to the surface. Another aspect of this growth is in the field of photoconductivity. Not only have extremely sensitive materials been developed which respond to low-level x-rays, but such materials have been developed in powder form particularly suitable for fabricating thin large-area devices.

About a year ago, an experimental x-ray amplifier was described (1) making use of electroluminescent and photoconductive materials. This amplifier demonstrated the feasibility of obtaining high brightness gains with a thin panel which could be directly viewed and whose amplifying action was not dependent on vacuum tube structures. Because of its potential applications some exploratory tests have been made recently as a means of evaluating it and as a guide in determining the direction of future developmental effort. Since the tests described below were made with early laboratory-constructed amplifiers, they should be considered only as indicative of the general possibilities of such panels rather than as exact criteria of their specific limitation.

PROBLEMS IN PRESENT FLUOROSCOPY

The need for increasing the brightness of a fluoroscopic image insofar as it concerns inconvenience in viewing needs no emphasis. However, the inability of the radiologist to perceive picture information on the screen because of the low-

level image is of a more serious nature. This problem was thoroughly studied by Chamberlain (2) many years ago, and some of his conclusions can be briefly summarized.

In clinical practice, the brightness of the typical fluoroscope screen is between 0.0001 and 0.01 millilambert. A thick abdomen reduces the screen brightness to a level which is less than 1/10,000 that of a sheet of paper in normal reading light. At the low brightness levels of fluoroscopic work we are usually concerned with rod vision, which limits both acuity and intensity discrimination. In reducing the brightness of an image from 10 millilamberts (typical of ordinary room illumination) to 0.001 millilambert (typical of an 18-cm. abdomen in fluoroscopy), the visual acuity of the eye is reduced about fifteen times, *i.e.*, image details which can be separated by the eye must be fifteen times farther apart at the lower light level. At a viewing distance of 10 inches, for example, black and white contours separated by less than 1 mm. cannot be detected at 0.001 millilambert brightness.

A comparable limitation is the reduced ability of the eye to distinguish gross details of low contrast at low light levels. At 0.001 millilambert, intensity differences which exceed about 20 per cent of the background light are necessary for detection, whereas at 10 millilamberts, intensity differences of 2 per cent or less can be perceived. In actual fluoroscopic practice the eye is limited by a combination of both these handicaps, making the detection of small, low-contrast details particularly difficult.

The improvement in perception of image details expected from an increase in brightness has been confirmed in tests with image

¹ Accepted for publication in September 1958. The panel described here was developed at the RCA Laboratories, Princeton, N. J.

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amplifiers. With the Philips image intensifier, the smallest objects which can be seen are about half the size of those detectable on the ordinary fluorescent screen. Berridge and Guest (3) find, for example, that a copper wire 0.3 mm. in

these systems the x-rays must fall on a bulky vacuum tube structure, adding inconvenience to their routine use. In addition, because of their inherent design, all of these systems are relatively expensive.

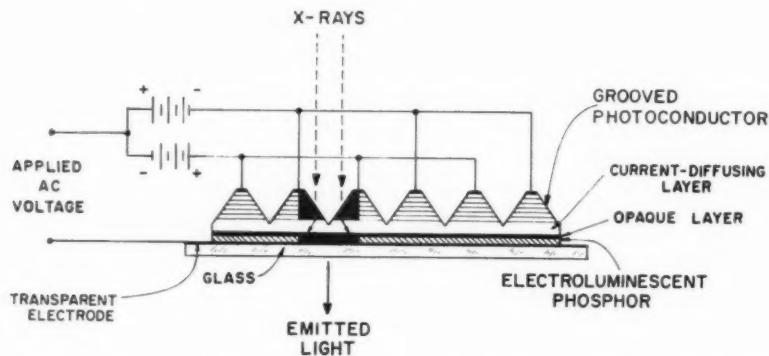


Fig. 1. Cross section of amplifying fluoroscope screen. (From Am. J. Roentgenol. 79: 712, April, 1958)

diameter can be identified in a 19-cm. phantom with the image intensifier (75-kvp. x-rays, 1 ma), while with the fluorescent screen a wire 0.7 mm. in diameter is required for identification (80-kvp. x-rays, 2.5 ma). These authors feel that with the ordinary fluorescent screen the mucosal pattern of the duodenal bulb can be seen only in thin subjects, but with the image intensifier it can be delineated clearly in all subjects. In addition, it has been found that the detail of the esophageal mucosa is easily visible through the dorsal spine with the image intensifier but not on the fluoroscopic screen.

Although the advantages of the image intensifier, as well as other types of image amplifying systems, have been generally recognized, their use has been restricted because of the many practical problems associated with them. With image intensifiers, the field of view is usually limited to a circle of about 5 in. diameter, while viewing is through an optical system or a TV chain. With both the Vidicon type (4) and Image Orthicon type (5) amplifying systems, relatively complex scanning and amplifying circuits are needed. In all of

DESCRIPTION OF THE PANEL AMPLIFIER

The solid-state amplifying panel avoids many of the practical objections mentioned above. In appearance it is a thin panel, about 1/4 in. thick and 12 in. square. In use it is positioned and viewed in a manner similar to the conventional fluoroscopic screen.

Figure 1 shows a cross section of the amplifier, exaggerated in thickness to indicate the construction. For practical purposes a glass base is used to support the layers. In operation the x-rays falling on the photoconductive layer increase its conductivity. This modulates the flow of A.C. currents through the corresponding areas of the electroluminescent layer which emits a bright pattern of light. (The opaque and current-diffusing layers are used respectively to prevent feedback of output light to the photoconductor and to assist in construction of the amplifier.) Details of the operation are more fully described elsewhere (1).

When excited, the amplifier integrates or builds up the x-ray image falling on it to produce an output image which can be viewed in moderate room illumination. This image is about 100 times brighter

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than the conventional fluoroscopic screen excited with the same x-ray level. The integration time may be as long as thirty seconds with low-level x-rays, or as short as a millisecond with high-intensity x-rays. For exciting the amplifier, the total exposure required is comparable to Kodak Blue Brand medical x-ray film.

With the x-rays cut off, the output decays slowly over a period up to thirty seconds, providing a temporary storage of the picture information. When desired, the long-decaying image may be interrupted or erased by electrical means and the amplifier excited with a new image. The resolution of the panel, with its present construction, is 40 lines per inch. For operation, power is provided by a portable supply connected to the panel with a thin cord.

The output image has a high gamma or contrast comparable to film with intensifying screens (1). At full voltage (about 600 volts) the latitude is also comparable to film with intensifying screens. However, for the tests described below, the amplifier was operated more conservatively (about 450 volts), with a consequent reduction in latitude.

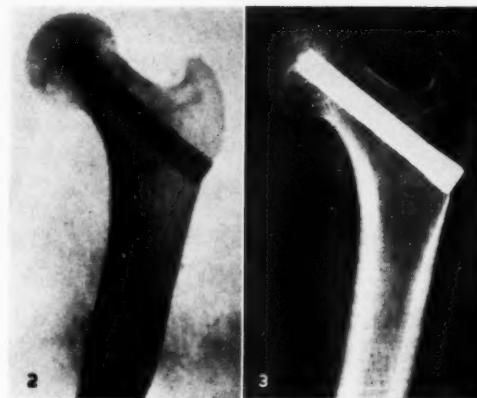


Fig. 2 Amplifier image of a 20-cm. Presdwood phantom containing an embedded femur, at 75 kvp.

Fig. 3. Conventional radiograph of 20-cm. Presdwood phantom containing femur.

TESTS WITH PHANTOMS

One phantom employed for evaluating the amplifier performance consisted of a dried femur centrally placed in 20 cm. of Presdwood. A Smith-Petersen nail was embedded in the femoral neck. Images were obtained on the amplifier from 60 to 250 kvp. The image produced at 75 kvp is shown in Figure 2. Figure 3 is a conventional radiograph of the phantom for comparison. Some of the reduction in image quality with the amplifier is



Fig. 4. Amplifier image using chest phantom at 100 kvp.



Fig. 5. Conventional radiograph of chest phantom at 80 kvp.

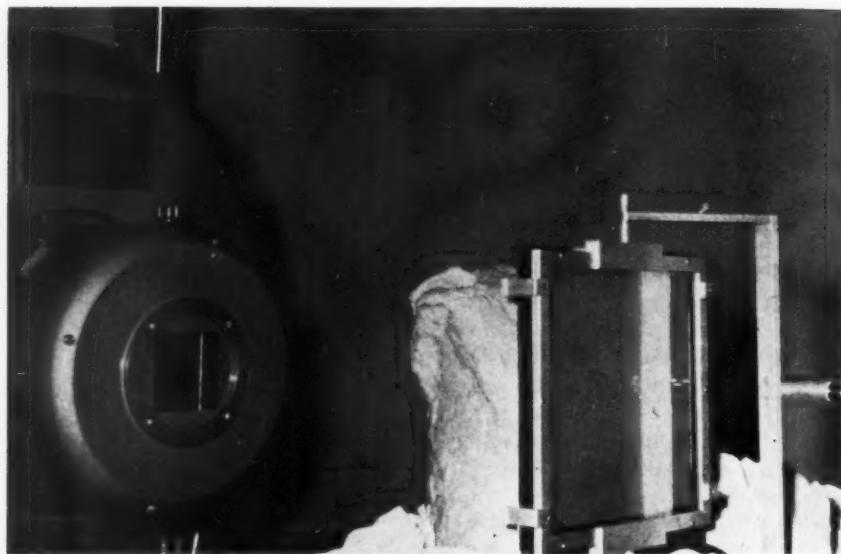


Fig. 6. Arrangement of amplifier panel, phantom, and 2-Mev source.

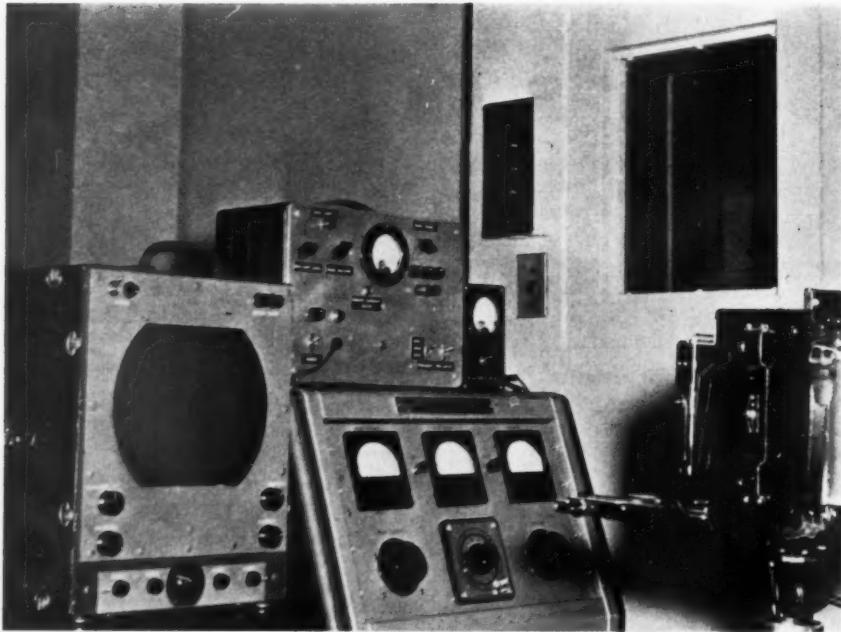


Fig. 7. Remote viewing screen and equipment controls.

caused by the present graininess and nonuniformities over the surface. In addition, the perception of fine detail is hindered by the resolution limitations of the amplifier due to its thickness and

grooved construction. The high contrast of the amplifier images results from the high gradient or gamma (approximately 3) of the amplifier characteristic.

The chest phantom developed by Harris,

Tuddenham, *et al.* (7) was also studied, the voltage range in this case being from 75 kvp to 2 Mev. Figure 4 shows a photograph of the amplifier output at 100 kvp. This can be compared to the conventional radiograph of the phantom shown in Figure 5, obtained at 80 kvp. All of the images of the chest phantom were obtained without a grid. The loss of picture information in the superior mediastinum is caused by the reduced latitude of the amplifier as operated in these tests.

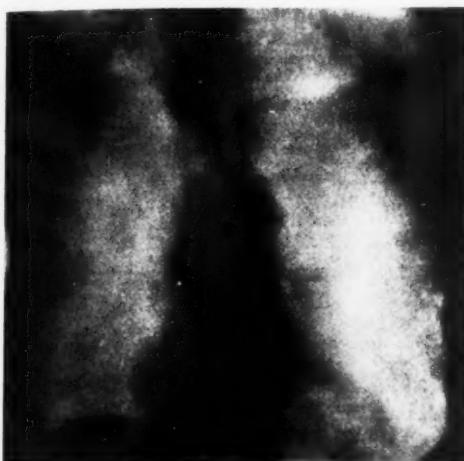


Fig. 8. Amplifier output with chest phantom at 2 Mev. Photographed from TV tube.

At 2 Mev the output image, using the chest phantom, was picked up by a Vidicon camera and displayed remotely on a TV tube. Figure 6 shows the physical arrangement of the amplifier panel, phantom, and 2-Mev Van de Graaf source. The remote TV screen is shown in Figure 7 adjacent to the x-ray control unit. Above the control unit is the portable supply for the panel amplifier. At the right is the camera for recording the TV picture. Figure 8 is a photograph of the amplifier output as seen on the TV tube face.

TESTS WITH PATIENTS

Because of the long decay period of the present amplifier, moving images cannot be viewed. This decay, however, is of



Fig. 9. Amplifier image on TV screen of a hypopharyngeal area at 2 Mev. See darker central area in Fig. 10.

value in certain applications where image storage is desired. In portal radiography, for example, it is not only advantageous to have an immediate image of the therapy portal with adequate brightness, but it is also advantageous for the image to persist for an extended time with the x-rays off. This permits either viewing the amplifier image directly through the lead glass window of the therapy room or at close range by entering the room during the decay of the image with the x-rays off. A convenient alternative, especially at higher voltages, is to use a Vidicon camera to pick up the amplifier image and display it remotely outside the treatment room.

Figure 9 shows an image of the therapy portal of the hypopharyngeal area obtained at 2 Mev as photographed from the remote TV display unit. The portal film of the pharynx, also using 2 Mev, is shown in Figure 10. As expected, the contrast between air and soft tissue is greater than between the soft tissue and



Fig. 10. Portal film at 2 Mev of patient of Figure 9.

bone. Despite some loss in image quality in passing through the TV chain, the image on the amplifier, although reversed in polarity, is comparable in contrast to the portal film.

In general, insofar as portal radiography is a supplemental procedure and reference may be made to previously obtained diagnostic films, a less critical image quality is acceptable. Although the present amplifier is grainy and exhibits non-uniformities, it is believed capable of adequately delineating anatomical landmarks. Of particular advantage is the fact that it can be used without changing the factors selected for treatment, building up a bright image in a few seconds or less. The time delay inherent in obtaining and processing portal films can thus be eliminated.

To explore the feasibility of utilizing the panel amplifier in operative procedures, as, for example, in hip pinning, a group of tests were made on postoperative patients. Figure 11 is a postero-anterior view of the right hip as photographed from the amplifier panel. Figure 12 shows the same image as recorded by conventional radiography.

An additional problem noted in these

tests is the excessive current flow through areas of the panel where there is little or no x-ray absorption by interposed tissue. This causes a reduction in the panel voltage (unless specially designed or much larger power supplies are used) which further reduces the latitude of the amplifier compared to film. The loss of halftones in the extremes of dark and light areas of Figure 11 was caused by a drop in panel voltage of about 100 volts in these tests. The excessive current flow also results in local heating and may damage the amplifier. Although one solution for this is accurate coning, this is inconvenient because of the arbitrary shapes of the masks or cones required. A better solution would be to provide a means of electronic limiting or self-protection within the panel itself.

In diagnostic work, the total x-ray exposure to the patient is of greater relative importance than in therapy. While the present panel is comparable to Kodak Blue Brand medical x-ray film in exposure requirements, further improvement to reduce the exposure to the level used with intensifying screens is desirable.

DISCUSSION

The present experimental amplifier is indicative of the possibilities of such solid-state devices for the future. With the advantage of its physical form and simplicity of operation, its continued development may ultimately provide the ideal x-ray amplifier. Below are set down some of the objectives which it is believed should be satisfied to make it useful in all types of medical applications. These are grouped below into three categories. Group I includes characteristics presently possessed by the amplifier. Group II includes properties which might be obtained by engineering modifications and improvements. Group III lists characteristics whose attainment is much less certain and which are dependent on the results of long-term research and development of new materials.

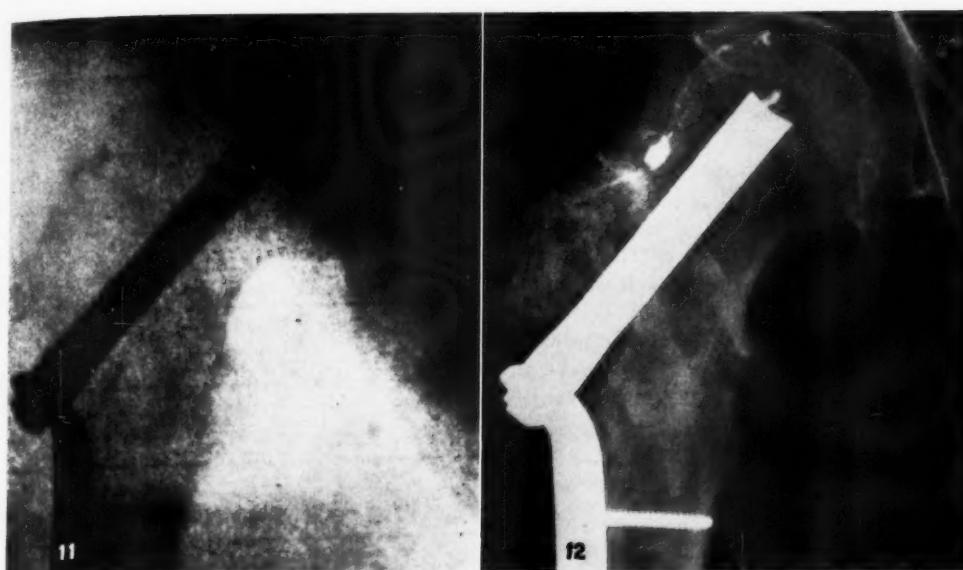


Fig. 11. Postero-anterior view, on amplifier, of patient following hip pinning.
 Fig. 12. Conventional radiograph of patient of Figure 11.

Group I

1. Large-area, thin panel, light in weight
2. Simplicity of operation
3. Easily adaptable to existing equipment
4. High amplification factor
5. High contrast
6. Image storage of limited duration

Group II

1. Resolution comparable to fluorescent screens or better
2. Brightness of 10 millilambert or greater for viewing in all types of room light
3. Contrast and latitude variable at will
4. Usable with film as a substitute for intensifying screens to reduce exposure

Group III

1. Reduction of grain and nonuniformity to level of fluoroscopic screen or better
2. Response time of 1/64 sec. for viewing fast motion

3. Reduction of input exposure requirements down to limitation imposed by quantum noise of x-rays
4. Storage of half-tone images for an arbitrary time, and capability of integrating or building up very low-level images

The attainment of characteristics 2 and 3 of Group III with amplifiers of the present form requires orders of magnitude improvement of present materials. An interesting possibility for the future may lie in the use of ferroelectric materials which might offer a means of providing long storage and at the same time increasing the gain of the amplifier.

CONCLUSION

X-ray amplifying panels have been tested over a wide range of voltages to determine their usefulness where stationary images are involved. In portal radiography in areas where high contrast exists, the image quality of the amplifier is adequate to permit localization of the treatment area with the therapy beam. In diagnostic work, although useful images can

be obtained, several problems are noted: (a) the graininess of the image interferes with the discrimination of small half-tone differences; (b) the latitude of the amplifier is less than with conventional radiographs when it is operated below 600 volts (an upper practical limit); (c) in images where a large difference exists in x-ray transmission some areas of the amplifier are excited beyond a safe level, with possible heating and breakdown. It is believed, however, that with limited improvements the usefulness of such panels may be further extended.

ACKNOWLEDGMENT: The support and encouragement of Mr. E. W. Herold and Dr. I. Wolff in the panel development work are appreciated, as well as discussions with Dr. D. W. Epstein. We wish to express grateful appreciation to Dr. E. P. Pendergrass for his support in making possible tests at the University of Pennsylvania Hospital. Helpful assistance and advice were also provided by Drs. P. J. Hodes, R. H. Chamberlain, and A. Raventos. We are indebted to Dr. W. J. Tuddenham for the loan of

the chest phantom. Additional aid was provided by Mr. J. Bernath in the fabrication of the amplifier panels and by Mr. J. E. Berkeyheiser in tests with the panels.

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SUMARIO IN INTERLINGUA

Resultatos Experimental Obtenite con le Amplificador de Radios X in Forma de Pannello

Un amplificador experimental de radios X, a forma de pannello e utilisante materiales electroluminescente e photoconductive, ha previamente esseite describite (Am. J. Roentgenol. **79**: 709, 1958). Iste amplificador ha nunc esseite testate con extense variationes de voltage pro determinar su utilitate in le caso de imagines stationari.

In le radiographia portal in areas a alte contrasto, le qualitate del imagine in le amplificador es adequate pro permitter le localisation del area de tractamento con le fasce therapeutic. In studios diagnostic, ben que imagines de valor pote esser obtenite, plure problemas es a notar: (1) Le

character graniforme del imagine obstrue le distinction de micre differentias de nuance. (2) Le latitude del amplificador es minus que le latitude de radiographias conventional quando illo es activate a infra 600 volt (e pro rationes practic, 600 volt es un limite superior). (3) In imagines in que il existe grande differentias de transmission de radios X, certe areas del amplificador es excitate in ultra de nivellos salve, con le resultado possibile de hypercalefaction e panna. Nonobstante, le opinion es exprimate que meliorationes non troppo extense va resultar in un augmento del utilitate de tal pannellos.

Radiation Reduction by Combined Copper and Aluminum Filtration in Radiography¹

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HERMAN CEMBER, M.S.,⁵ CHARLES R. GRIFFITH, M.S.,⁶ and LAWRENCE C. CROSS, R.T.⁷

HERE HAS BEEN increasing anxiety among laymen as well as the medical profession concerning genetic damage from x-rays. Much has been written on the subject (1) and progress has been made in dispelling some of the hysteria arising from publication of reports of mutations, etc. (2). Radiologists are being asked by their colleagues about doses of radiation in various radiographic procedures. For informative answers to these inquiries more factual data are needed.

Conventional techniques for various examinations were compared with those utilizing 2 and 3 mm. aluminum filters combined with various thicknesses of copper. With the combination filters, radiographs of a better range of tonal quality and visibility of details were obtained, and radiation to the parts examined as well as to the gonads was markedly reduced. For example, films of the paranasal sinuses were made with an 8:1 grid, detail screens, regular film, diaphragm, and cylinder. As is apparent in Figure 1, these showed excellent detail and lack of excessive contrast. Soft tissues of the nose are seen along with details in the base of the skull, due, it is believed, to a higher quality beam with less differential absorption. Doses to the skin and gonads are shown in Figure 2.

Most of our dosage measurements were made on mannikins⁸ designed to simulate

the composition and size of the human body, with paraffin in the trunk and limbs and polyethylene bottles in the thorax. Wells were embedded in the pelvis at the anatomical location of the ovaries so that ionization chambers⁹ could be introduced for measurements. Lincoln and Gupton(3) used these techniques to determine dosages to the gonads in various typical x-ray examinations. Doses to the testes were measured directly in many cases with dosimeters adjacent to the scrotum.

We have used all the well known means of reducing dosage, such as long focus-film distance, smallest possible cones, a diaphragmed beam, fast screens and films, as well as accelerating processing chemicals, in order to achieve the lowest possible dose. From aluminum penetrometer studies, we have found the widest range of tonal qualities on film with a combination filter of copper and aluminum (4), and a marked additional reduction in radiation dosage has been obtained by this means. This is especially so with reference to skin dose. Using a combination of 0.375 mm. copper and 3.0 mm. aluminum, we achieved a reduction of 88 + per cent in dosage at the table top and to the patient's skin in conventional fluoroscopy (Fig. 3). At 90 to 100 kv, the brightness of the screen is not reduced appreciably and the spot films (at 120 kv) are of excellent quality. With

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⁸ The first of these was loaned to us by Dr. Thomas A. Lincoln of Oak Ridge, Tennessee. Our mannikin was filled with Columbia wax or paraffin, having a specific gravity of 0.93 and a density similar to that of the human body. Polyethylene bottles filled with air, one liter each, were placed in the chest cavity.

⁹ Victoreen thimble chambers of both 25 and 100 r ranges were used in these measurements and were checked at the factory against the radiation physicist's meters. Landsverk Dosimeters of 200 mr capacity and also Tracerlab meters were checked against Victoreen standard thimble chambers.

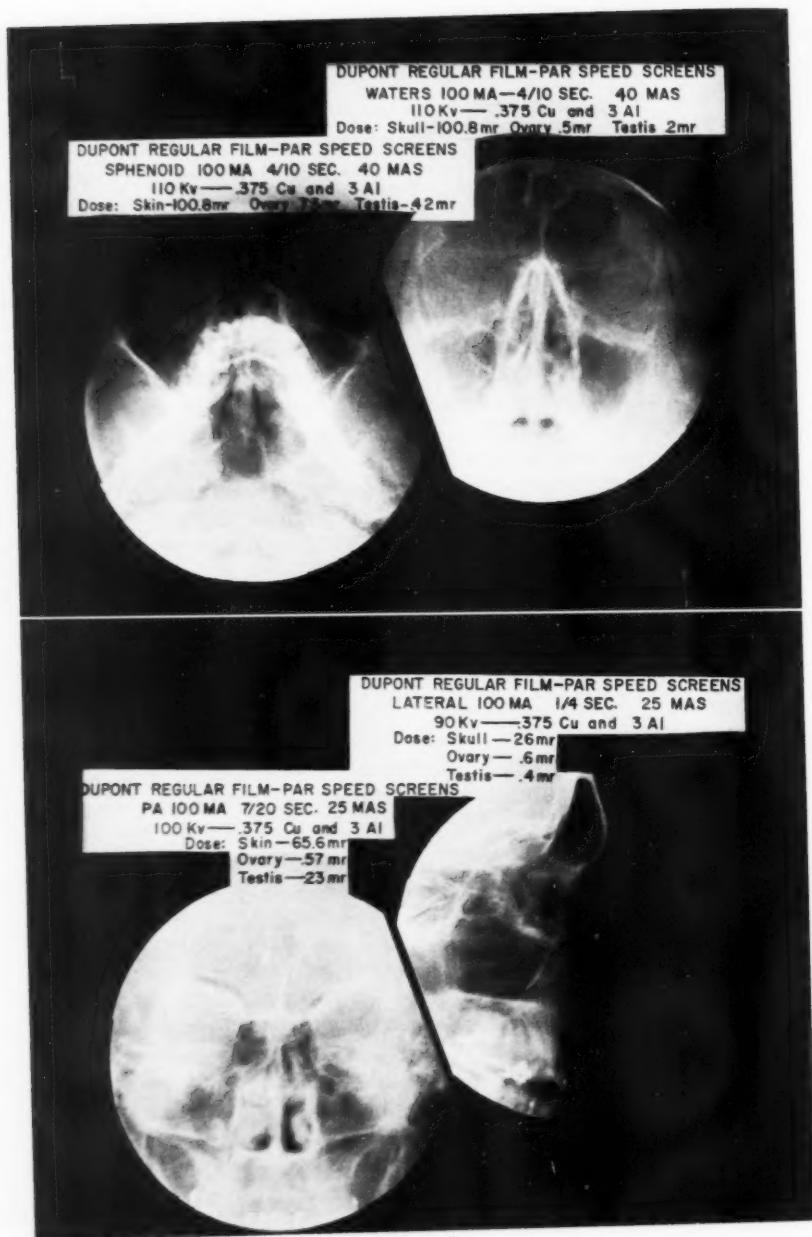


Figure 1.

the image amplifier at 90 and 100 kv and 1 ma current (Fig. 4), and a scanning technic as for upper gastrointestinal examinations, a very low skin dose was obtained with addition of 0.375 mm. of copper to the inherent filter in the tube plus 1 mm. equivalent

value of aluminum for the table top. The doses to the gonads were extremely low, being reduced almost to the vanishing point by addition of the copper filter.

Definite reductions were also obtained in both skin and gonad doses in radiography of

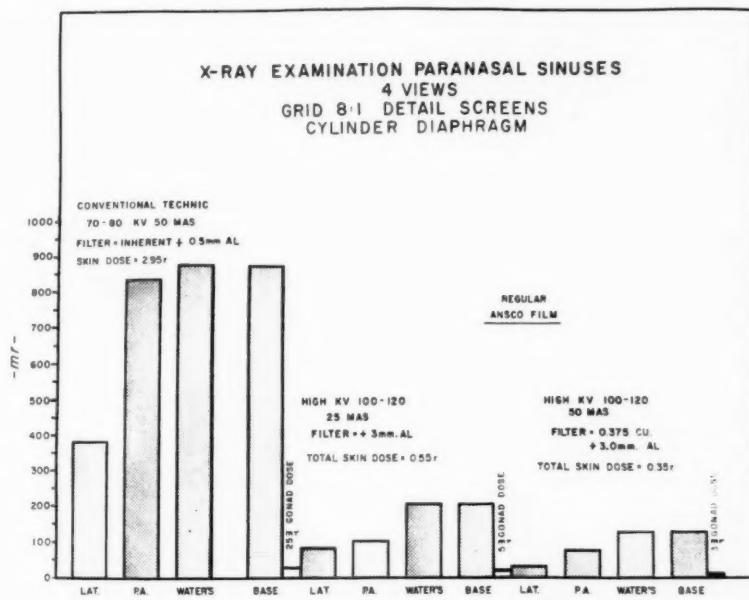


Figure 2.

TABLE I: BONE MARROW DOSE REDUCTION

h.v.l.	Measured Skin Dose	Depth (F.S.D.)	Depth at 5 cm.	Percentage Dose*	
				at 5 cm.	Based on 2 mm. Al h.v.l.
2 mm. Al	10.2 r/min.	33%	3.4 r/min.	0	
4 mm. Al	7.4 r/min.	44%	3.2 r/min.	6%	
0.8 mm. Cu	1.5 r/min.	62%	0.9 r/min.	76%	

* Depth dose data taken from John's *Physics of Radiation Therapy*.

We have decreased the skin dose by a considerable factor by using the copper filter, whereas we have increased the percentage depth dose. Multiplying a higher percentage depth dose by a lower value skin dose gives a resultant lower net depth dose.

the skull, abdomen, and chest (Figs. 5-7). A comparison was made of dose reductions obtainable with various types of screen (Fig. 8). It will be seen that the greatest relative reduction in dose with increased filtration occurred with the detail screens.

By using a combination of fastest available film, high-speed screens, high kilovoltage, accelerating processing chemicals, and progressively more filtration, a further

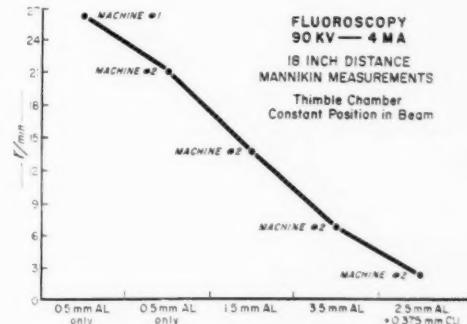


Figure 3.

considerable dose reduction to skin and gonads was obtained in a lateral skull x-ray examination (Fig. 9).

Of greatest importance is a consideration of depth doses in the various tissues and the bone marrow (5). With the above described combination of copper and aluminum filters, there is a lowered depth dose because, with the higher quality beam, even though the percentage depth dose is increased, the skin dose is so low that the net dose to the deep tissues is reduced, as shown in the accompanying table.

Our findings in cineradiography with the

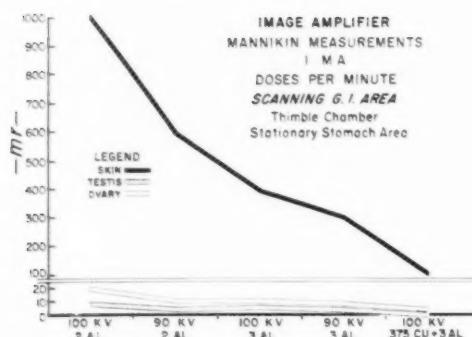


Figure 4.

mannikin are illustrated in Figure 10. A scanning technic was used as with examinations of the upper gastrointestinal tract. In addition to measurements on the mannikin, we made direct measurements adjacent to the gonads in male patients during cinefluorography. Whereas in this procedure at 100 and 120 kv, in a constant position, the dosage without filtration is quite high, we found that scanning, with 0.375 mm. of copper and 1.5 mm. of aluminum, resulted in an average gonadal dose of only 5 mr per minute of operation. With a 3-mm. aluminum filter alone, the dose averaged 8 mr per minute.

In our particular set-up, we were obliged to figure at least a total of 1.5 mm. aluminum in fluoroscopy, allowing 0.5 mm. of aluminum for inherent tube filtration and 1 mm. aluminum equivalent, quite surprisingly, for the table top. This latter measurement was made by first removing the table top and positioning the chamber exactly as it would be if the table top

were there. At 100 kv, 5 ma, and with 1.0 mm. of aluminum filter added, we measured an output of 8.7 r per minute at 30 cm. from the tube. Knowing that our reading with the table top without the phantom was 8.9 r/min., we concluded that the equivalent value of the table top was

REGULAR FILM PAR SPEED SCREENS

AP ABDOMEN

	2 AL 62 KV 50 MAS	3 AL 100 KV 50 MAS	.375 CU 100 KV 40 MAS	.375 CU 3 AL 100 KV 50 MAS
SKIN	331 MR	260 MR	145 MR	139 MR
OVARY	42.7 MR	33 MR	24.6 MR	23 MR
TESTIS	77.9 MR	26 MR	24.3 MR	21.4 MR

Figure 6.

approximately 1.0 mm. aluminum. We had been told, and the manufacturers apparently assumed, that the table top equivalent was about 0.5 mm. of aluminum. This finding shows the importance of checking these factors in a given installation.

We have shown from the radiographic standpoint that in many areas of examination a better range of tonal quality can be achieved by a combination of copper and aluminum filtration in the x-ray beam. With this improvement, there is a tremendous reduction in radiation dosage to the skin and, incidentally, a resultant lowered depth dose made possible by the higher quality beam. This results in lower bone-marrow dose as well as decreased dosage to

REGULAR FILM PAR SPEED SCREENS

PA SKULL

	2 AL 70 KV 50 MAS	3 AL 110 KV 15 MAS	.375 CU 110 KV 25 MAS	.375 CU 110 KV 30 MAS
SKIN	400 MR	225 MR	200 MR	180 MR
OVARY	3 MR	.3 MR	.06 MR	.05 MR
TESTIS	.3 MR	.02 MR	.02 MR	.01 MR

Figure 5.

REGULAR FILM PAR SPEED SCREENS

PA CHEST

	2 AL 64 KV 10 MAS	3 AL 95 KV 5 MAS	.375 CU 95 KV 7.5 MAS	.375 CU 95 KV 10 MAS
SKIN	16.7 MR	12 MR	8.3 MR	6.7 MR
OVARY	.2 MR	.05 MR	.04 MR	.03 MR
TESTIS	.08 MR	.005 MR	.002 MR	.001 MR

Figure 7.

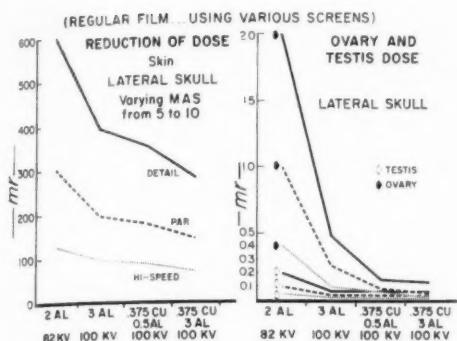


Figure 8.

the gonads, and is especially significant in conventional fluoroscopy, image amplification fluoroscopy, and in cinefluorography.

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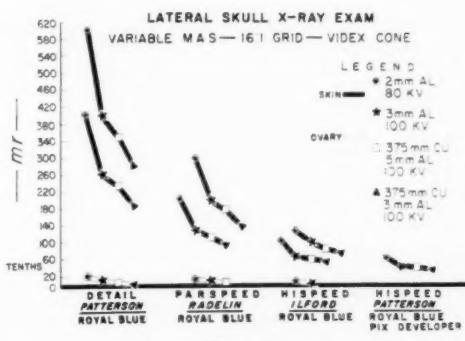


Figure 9.

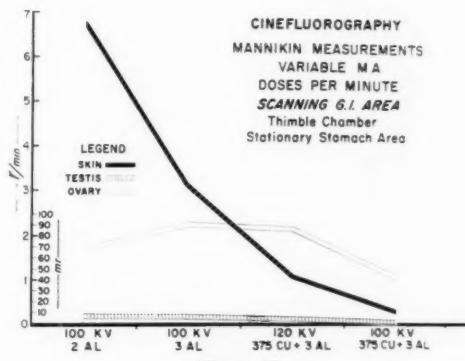


Figure 10.

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SUMMARIO IN INTERLINGUA

Le Reduction del Radiation in le Radiographia per le Uso de Filtration per Cupro e per Aluminio in Combination

Es monstrate ab le punto de vista radiographic que in multe areas de examine un meliorate scala de qualitate tonal pote esser effectuate per le uso combinante de filtration a cupro e a aluminio in le fasce de radios X. Iste melioration resulta in un reduction tremende del dosage de radiation al pelle. Concomitantemente le meliorate

qualitate del fasce rende possibile un reduction del dosage de profundor. Le consequentia es un reduction del dosage al medulla ossee e etiam del dosage al gonades. Iste reduction es specialmente significative in fluoroscopia conventional, in fluoroscopia a amplification de imagine, e in cinefluorografia

Primary Reticulum-Cell Sarcoma of the Spleen

Report of a Case Presenting as a Cyst¹

NIMR A. TUQAN, M.D., and GEORGE W. SALEEBY, M.D.

PRIMARY SPLENIC neoplasms are of unusual occurrence (2). On reviewing 11,707 autopsies and 68,820 surgical specimens, Bostick (1) encountered only 7 cases. Such tumors are derived from endothelium, lymphoblasts, reticulocytes, fibroblasts, smooth muscle, mesothelium,

being primary in the spleen. In this respect, two points are worth mentioning:

1. The only diagnostic criterion of a primary lymphoma of the spleen is the absence of any extrasplenic lymphomatous lesion at the time of recognition of the splenic tumor.

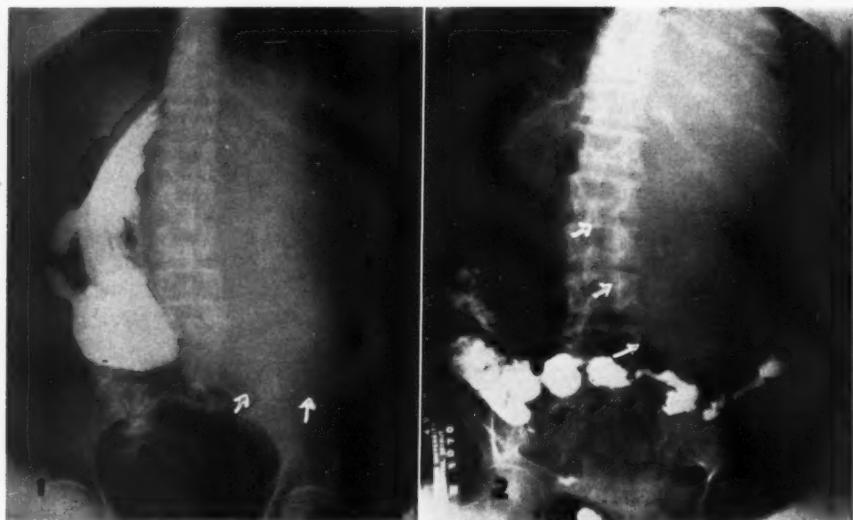


Fig. 1. Displacement of the stomach to the right. Its greater curvature is a concave arch representing the right border of the cyst. Arrows point to the interior border.

Fig. 2. Displacement of the colon downward. Arrows point to the medial border of the cyst.

and embryonic inclusions (1). Malignant variations are rare. Langenstrass (4) encountered a single primary sarcoma in 6,400 autopsies. Primary malignant lymphomas though certainly uncommon, comprise a considerable portion of the primary tumors of the spleen (5).

The organ of origin of solitary or multiple lymphoma which in the advanced stages has become diffuse in the reticuloendothelial system may go unrecognized. In these advanced stages one loses the criteria that distinguish a lymphoma as

2. Late secondary involvement of the spleen in a case of lymphoma is usually diffuse. Limitation of the disease to part of the spleen, while there is evidence of diffuse lymphoma in other organs, is suggestive, *but not diagnostic*, of a primary splenic lymphoma.

In view of such criteria, one is inclined to be hesitant in accepting as genuine some of the reported cases of reticulum-cell sarcoma primary in the spleen (3).

Splenic cysts, like splenic tumors, are also rare. Textbooks classify them as

¹ From the Departments of Pathology (N. A. T.) and Radiology (G. W. S.), American University of Beirut, Beirut, Lebanon. Accepted for publication in August 1958.

single or multiple, true (with a lining) or false (without a lining), lymphangiectatic, hemangiomatous, hydatid, dermoid, post-traumatic, and post-infarction. No classification was found that includes lymphoma as an underlying cause of cyst formation.

Our purpose in this report is twofold: (a) to present a case of primary reticulum-

reaching 38.5°C . During her illness she lost weight and felt very weak. The only other symptoms were a tendency to constipation and frequent gaseous distention relieved by eructation or passage of gas per rectum.

Physical Examination: On admission the patient appeared weak and emaciated. The skin was pale and dry and the tongue was raw and red. The chest moved freely. The pulse was 100, the heart sounds were regular, and a soft systolic murmur was heard. The blood pressure was 125/65. A mass

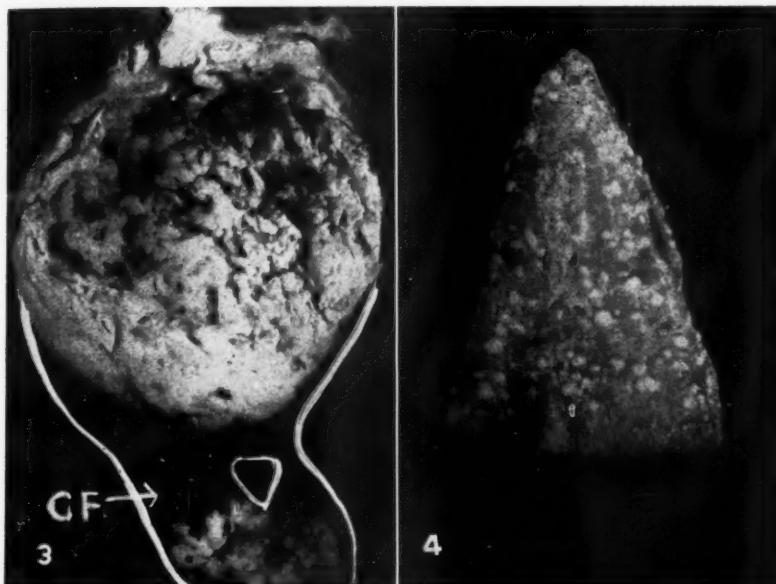


Fig. 3. Two tumors in the spleen. The center of the larger one is cystic. It collapsed after removal of 3,500 c.c. of hemorrhagic fluid. The tissue between the two tumors is the red pulp containing prominent white pulp. G.F. points to a giant follicle. The splenic tissue enclosed within the triangle contained hyperplastic white pulp.

Fig. 4. The white pulp contained within the triangle in Fig. 3, under magnification.

cell splenic lymphoma breaking down to produce a large pseudocyst; (b) to describe the peculiar clinical, radiologic, and operative features of this tumor, thus drawing attention to a diagnostic and prognostic pitfall in the management of apparently benign cysts of the spleen.

CASE REPORT

Clinical History: The patient was a 50-year-old housewife whose illness began two years prior to admission with a sensation of a shifting mass in the left lower abdominal quadrant. This was more apparent upon change of position. After eight months, a nontender, painless mass became palpable in the same region. Five months prior to admission the patient began to experience daily chills and fever

with a smooth surface filled the left abdomen from the costal margin to the iliac fossa, moving slightly with respiration. Superiorly, it seemed to be directly under the abdominal wall and fixed to it. There was slight tenderness in the left costovertebral angle. There were no other abdominal findings of significance. Pelvic examination revealed fullness and tenderness in the left lower quadrant, too distant to be related to the pelvic organs. Neurological examination was essentially negative.

Radiologic studies showed a mass in the left side of the abdomen extending from the diaphragm to the left iliac bone inferiorly and crossing the midline to the right. It was of uniform density, with a sharp border, and measured 22 cm. in diameter. A barium meal examination showed no lesion in the digestive tract, but the stomach was displaced to the right and the greater curvature formed a concave arch along the right side of the spine, as a result of the

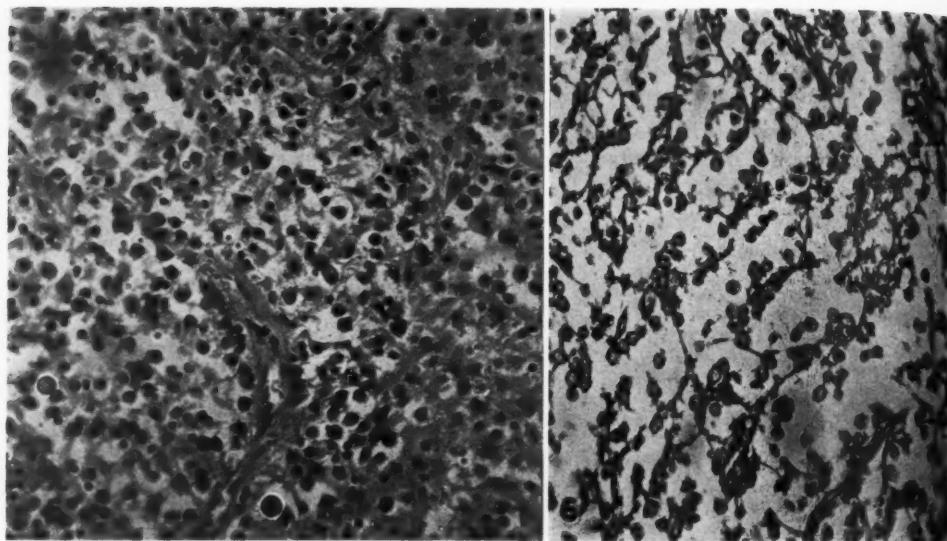


Fig. 5. Typical reticulum-cell sarcoma. Hematoxylin-eosin. $\times 300$.
 Fig. 6. Typical reticulum-cell sarcoma. Stained with Wilder's technic to show reticular fibers. $\times 300$.

impinging spherical mass (Fig. 1). The transverse colon was displaced downward below the level of the iliac crest (Fig. 2).

An electrocardiogram showed a deviation of the axis 22° to the left, which was interpreted to be the result of ventricular enlargement or a high diaphragm on the left side.

The laboratory findings were: red cell count 3,600,000; hemoglobin 12.6 gm.; white cell count

8,600 with 80 per cent polymorphonuclears, 8 per cent lymphocytes, 6 per cent large monocytes, 6 per cent eosinophils; urea nitrogen 14 mg. per cent; sugar 86 mg. per cent; chlorides 510 mg. per cent; protein 6.6 gm. per cent; albumin 4.6 gm. per cent; globulin 2 gm. per cent; serum amylase 80 units; icteric index 5; Wassermann and Weinberg tests negative. The urine was acid, of 1.013 specific gravity, with a trace of albumin and no sugar. There was an occasional white blood cell in the sediment; phenolsulfonphthalein 60 per cent.

Exploratory laparotomy showed the mass to be a greatly enlarged spleen filling the whole of the left side of the abdomen and crossing the midline. It was adherent to the liver, omentum, intestines, and diaphragm and contained 3,500 c.c. of hemorrhagic fluid. After aspiration, splenectomy was performed. The fluid did not yield any organisms on culture.

Pathology and Comment: Gross examination of the specimen showed a spleen measuring $30 \times 20 \times 20$ cm. The enlargement was due to the presence of two masses within the substance of the organ. The larger one, situated in the region of the superior pole, had a collapsed cystic center measuring 18 cm. in diameter. The tissues surrounding the cyst were homogeneous, soft, and white, and measured 4 to 6 cm. in thickness. The other mass was situated in the inferior pole. It was composed of similar but solid tissue and measured 10 cm. in diameter (Fig. 3). The area between these two masses showed firm splenic tissue, with scattered spots of prominent white pulp (Fig. 4).

Histologic examination of the cyst wall and the solid mass revealed complete alteration of the splenic architecture and replacement of the normal tissues



Fig. 7. Section from between the two tumors showing the red pulp, with preservation of architecture, separating a small follicle of white pulp and a giant follicle.

by a mesenchymal cellular growth (Fig. 5). The cells were identified as of the reticulum type. A differential Wilder's stain showed the formation of fine argyrophil fibrils closely related to the tumor cells (Fig. 6). The neoplasm was diagnosed as a reticulum-cell sarcoma.

The breakdown of tissues of the larger mass transformed it into a pseudocyst.

The presence of two histologically similar masses and the numerous hyperplastic white pulp nodules suggested that the tumor was of multicentric origin. It probably arose as a giant follicular lymphoma (Figs. 4 and 7).

Since there was no evidence of an extrasplenic lymphoma at the time of recognition of the splenic tumor, the case was considered as primary reticulum-cell sarcoma of the spleen.

Course and Follow-up: Following operation severe anemia developed and there was evidence of recurrent tumor in the left diaphragmatic region. Death occurred eighteen months postoperatively (four years after the onset of the illness) with pleural effusion and signs of rib destruction.

SUMMARY

1. A case of reticulum-cell sarcoma of the spleen is presented.

SUMMARIO IN INTERLINGUA

Primari Sarcoma Reticulo-Cellular Del Splen: Reporto De Un Caso Presentate Como Cysto

Es presentate un caso de sarcoma reticulo-cellular del splen. Le tumor esseva de origine multicentric e pareva haber comenciate in le splen como un gigante lymphoma follicular. Le collapso de histos

2. The tumor was of multicentric origin and appeared to have arisen in the spleen as a giant follicular lymphoma.

3. The breakdown of tissues resulted in cyst formation, which produced certain peculiar clinical, radiologic, and operative features, masking the actual nature of the disease before histopathological identification.

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Fracture of the Hyoid Bone¹

C. G. PAPAVASILIOU, M.D.,² and C. J. SPEAS, D.D.S.³

FRACKURE OF THE hyoid bone is likely to prove fatal because of asphyxia. Sufficient stress to cause a hyoid fracture will frequently produce soft-tissue injuries which mask its presence unless the attending physician deliberately examines the bone radiographically, or familiarity with the clinical symptoms alerts him to its possibility. Conversely, the external visible evidence of a fracture or severe soft-tissue injury may be so slight that the possibility is overlooked. Patients may die because of asphyxia associated with pharyngeal and laryngeal spasm, unless relieved by tracheotomy.

The radiologic diagnosis of fractures of the hyoid bone has been neglected, only 8 cases having been reported in the last twenty to twenty-five years. Two cases to be presented here illustrate the clinical problems and the radiologic findings.

CASE I: Gunshot Fracture of the Hyoid Bone. A 23-year-old white male prisoner was struck in the left side of the neck by a single buckshot fired during a prison riot. The shot entered the neck about 1 cm. below the body of the mandible, near the angle, and passed through the body of the right mandible about 2 cm. anterior to the ramus, producing a fracture of the hyoid in its course across the neck. The patient was transported a distance of about 16 miles from the penal institution to the hospital. Hemorrhage and swelling in the neck were plainly visible. Dyspnea was marked and was relieved by tracheotomy. The fractured mandible was treated by wiring the teeth. Several small loose fragments were removed from the point of exit of the shot. No particular treatment was directed to the comminuted fracture of the cornu of the hyoid (Fig. 1). Convalescence was uneventful.

CASE II: Fracture of the Hyoid Bone from a Blow by a Fist. A 22-year-old white man became involved in a fist fight and sustained a fracture of the nose and hyoid bone. He was brought directly to the hospital from a short distance but was quite dyspneic on arrival. While he showed evidence of a



Fig. 1. Case I: Comminuted fracture of the greater cornu of the hyoid bone (arrow). Note the fracture of the mandible.

beating about the face and nose, the neck was not unusual in appearance. The patient could be relieved of his dyspnea by grasping his lower jaw, elevating his chin, pushing the jaw forward and putting his head in the Trendelenburg position. Complete relief was afforded by tracheotomy. In the roentgenograms of the facial skull and cervical spine, a fracture of the greater cornu of the hyoid bone close to its junction with the body was easily visible (Fig. 2). The tracheotomy tube was removed after about three days, and convalescence was uneventful.

SYMPTOMS AND SIGNS

Fractures of the hyoid bone are the result either of direct trauma, as strangulation, car accidents, or gunshot wounds, or of muscular action, as in sudden hyperextension of the neck or forcible deglutition. According to Olmstead (6), early bony union between the body and the greater cornua or anomalous ossification is a predisposing factor. The condition

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may be serious (2), with severe pain (accentuated by talking or swallowing), dysphagia, dysphonia, or severe dyspnea. Protrusion of the tongue produces suffocation. The fragments may penetrate the soft tissue of the pharynx and profuse bleeding may occur. Extensive subcutaneous emphysema may develop, as in our second case. In both of our patients dyspnea was the most prominent symptom, necessitating the insertion of a tracheotomy tube.

ROENTGEN FINDINGS

X-ray demonstration of a fracture of the hyoid bone requires no special views. Routine roentgenograms of the cervical spine demonstrate the bone satisfactorily. In the true lateral view, it is well seen through the soft tissue of the neck, although in this projection the two greater cornua are superimposed, one upon the other. In oblique views of the cervical spine, however, these two structures project one just above the other and can be seen clearly in their entire length. Superimposition of the cornua can also be avoided by a lateral view with the head slightly tilted to the side (7). An antero-posterior view of the neck is of no help, since superimposition of the hyoid on the cervical spine obscures the bony details. In a few cases, there is roentgen evidence of calcification and ossification of the stylohyoid ligament as well as of the thyrohyoid ligament. The latter observation was an incidental finding in one of our patients having no symptoms or complaints associated with the hyoid bone. Klinefelter (5) described a case of calcification of the stylohyoid and thyrohyoid ligaments associated with long styloid processes that produced symptoms mainly of pain and dysphagia.

The roentgen criteria of a fracture of the hyoid bone are (a) a radiolucent line; (b) interruption of the continuity of the cortex; (c) displacement of the fragments.

In more than half the reviewed cases, the fracture line involved the junction of the body with one of the greater cornua, and in

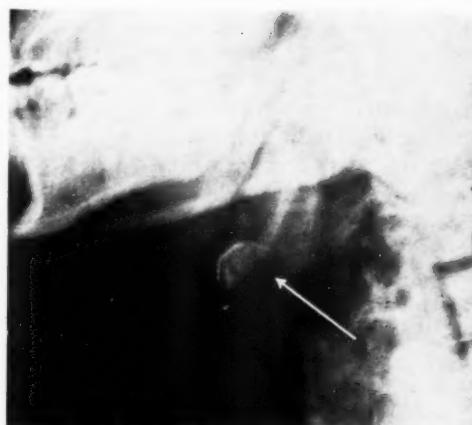


Fig. 2. Case II: Comminuted fracture of the greater cornu close to the junction with the body of the hyoid (arrow). Note subcutaneous emphysema.

the remainder the greater cornu itself. Tomizuka (9) states that fractures due to muscular action are prone to involve the distal tip of the greater cornu. No fractures of the body were identified in the reviewed cases. In each of our cases the fracture was comminuted.

In interpreting x-ray films of the hyoid bone several pitfalls should be avoided:

(a) It is easy to interpret as a fracture the normal line of radiolucency between the ununited body and greater cornu of the hyoid bone.

(b) The usually ununited lesser cornua may be mistaken for fragments of the hyoid bone.

(c) Sometimes only a small area of the thyrohyoid ligament, close to the hyoid bone, ossifies. This may be misdiagnosed as a fragment (8).

(d) Radiolucent lines due to air in the upper air passages of the neck might give the false impression of a fracture.

(e) In the oblique views of the spine, one cornu is slightly displaced above the other. This should not be interpreted as a dislocation.

COMMENT

Where injury such as has been described in the 2 cases reported above is seen in the emergency room, with the patient exhib-

iting dyspnea, the general practitioner, the internist, the otolaryngologist, the oral surgeon, the general surgeon, or anyone at hand should not hesitate to perform a tracheotomy immediately.

In the past, many cases of cancer of the lung were, no doubt, listed on death certificates as tuberculosis. By the same token, many deaths from fracture of the hyoid bone doubtless have been listed as death from suffocation.

It is imperative that the doctor examining a patient with an injury to the neck, jaws, face, or head, or even in the region of the clavicles, consider the possibility of a fracture of the hyoid bone. This injury, which produces not only difficulty in swallowing but marked respiratory embarrassment, may lead quickly to death. In the opinion of the authors the reason that so few cases of fractures of the hyoid bone are on record is that many of these patients die of suffocation shortly after the injury and are never examined roentgenologically. The fracture is not found on autopsy or, if found, is not listed as the cause of death.

In automobile accidents, where the head is thrown forward and the neck strikes the steering wheel, dashboard, or back of the front seat, fractures of the hyoid bone result far more often than the literature would indicate. It is no doubt true that many patients can compensate rapidly for these fractures, obtaining enough air and swallowing well enough to keep from strangling; others cannot compensate as quickly; many have had a mild concussion and loss of reflexes, and death ensues

promptly unless a tracheotomy is performed without delay.

SUMMARY

1. Two cases of fracture of the hyoid bone diagnosed clinically and radiologically are added to the scanty literature on the subject.
2. Some pertinent data concerning the roentgen demonstration of these fractures and the pitfalls to be avoided are presented.
3. The necessity of immediate tracheotomy is emphasized, since asphyxia frequently follows this injury.

ACKNOWLEDGMENT: The writers are grateful to Dr. Robert P. Ball for his advice.

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SUMARIO IN INTERLINGUA

Fractura del Osso Hyoide

Duo casos de fractura del osso hyoide es addite al sparse litteratura de iste thema.

Le fractura es demonstrabile in routinari expositiones lateral e oblique del spina cervical. Le criterios roentgenologic es (1) un linea radiolucente, (2) interruption del continuitate del cortice, e (3) displaciamiento de fragmentos. In plus que un

mediata del casos reportate, le linea del fractura coincideva con le junction del corpore del osso con un del cornos; in le resto del casos le fractura esseva in un del cornos mesme.

Dyspnea es un symptoma eminent. Si tracheotomia non es effectuate sin retardio, morte ab suffocation pote supervenir.

EDITORIAL

Clear Writing

One of the high spots of the 1959 College of Radiology Teachers Conference in Chicago was the discussion by a Mr. Robert Gunning on the subject "Clear Writing" (1). Those radiologists who attended will recall with pleasure his keen and amusing analysis of the good and bad in medical writing, and what to do about it.

All of us read medical articles and textbooks. Often we labor to understand an author's meaning, because it is buried in a mass of words and phrases which produce what Mr. Gunning called "fog." Clear writing includes use of sentences with an average of about fifteen words; avoidance of words of more than three syllables wherever possible; and the use of strong direct action verbs instead of verbal nouns ending in "ion" (e.g., "to help" instead of "implementation"). Straightforward writing intrigues as well as persuades the reader.

Simplicity in style does not imply monotony, however. The English language is so rich in words with many shades of meaning that choice of the exact word to convey the author's idea requires experience and skill. It is the precise use of words in a simple direct way that distinguishes the professional writer. The following discussion taken from Warren and Brooks (2) explains and illustrates the effect of sparkling words in simple settings.

"An inexperienced writer tends to overload his description with adjectives with the idea of specifying all the qualities of the thing being presented. Such a writer forgets that suggestion is often better than enumeration and that the mere listing of qualities is not the best way to evoke an image in the reader's mind.

"Let us look at the following portrait:

"The woman's face was fat and shapeless, so fat that it looked soft, unresilient,

grayish and unhealthy. The features were blurred because her face was fat. But her small, black, glistening eyes had a quick inquisitive motion as they moved from one face to another. . . .

"Let us now take the passage as William Faulkner originally wrote it before we tampered with it:

"Her eyes, lost in the fatty ridges of her face, looked like two small pieces of coal pressed into a lump of dough as they moved from one face to another. . . ."

Editors and publication committees of medical journals are flooded continually with badly written papers. Usually the authors of these papers have something to say (and it may be important), but they are so long coming to the point and their composition, style, and even grammar are so fumbling that the reader becomes discouraged before he is halfway through.

A thoughtful critic (3) has suggested that "anyone writing for scientific purposes ought to become familiar with the five basic elements that have been worked out, over the years, by the journalistic profession." These include putting the most important information in the opening paragraphs of a paper; prefacing the whole story with a brief summary on the front page (e.g., the J.A.M.A.); more frequent use of the first person, especially when there are two or more authors ("we found, etc."); writing in an informal manner which wins friends among readers; using drawings and charts (film reproductions) with clear self-explanatory captions, to break up the monotony of the written word and retain reader interest.

In almost all medical articles the authors could say everything that is necessary in half the number of words. Case reports could be shortened by omission of insignifi-

cant laboratory findings and clinical observations that have no bearing on the diagnosis, or at least these could be briefly summarized. Reviews of the literature could be drastically cut. Occasionally, it is true, these are of value, but too often the author feels it incumbent upon him to preface his own observations with an exhaustive account of the work of his predecessors, when a few well chosen words, with appropriate references, would be entirely adequate.

From time to time one reads about the "dos and don'ts" of public speaking on

medical subjects (4). In medicine, there are many more writers with captive audiences, than speakers. At long last, we captive readers should demand better stuff.

ROBERT P. BARDEN, M.D.

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ANNOUNCEMENTS AND BOOK REVIEWS

ARKANSAS RADILOGICAL SOCIETY

The Arkansas Radiological Society recently elected the following officers for the ensuing year: President, E. A. Mendelsohn, M.D., Fort Smith; Vice-President, E. M. Cooper, M.D., Jonesboro; Secretary-Treasurer, J. B. Scruggs, M.D., Arkansas Baptist Hospital, Little Rock; Councilor to the American College of Radiology, J. D. Calhoun, M.D., Little Rock.

TENNESSEE RADILOGICAL SOCIETY

At a recent meeting of the Tennessee Radiological Society, the following officers were elected: President, Granville Hudson, M.D., Nashville; President-Elect, George K. Henshall, Jr., M.D., Chattanooga; Vice-President, Edward H. Mabry, M.D., Memphis; Secretary-Treasurer, James J. Range, M.D., P. O. Box 324, Johnson City; Member of the Executive Committee, Charles Reavis, M.D., Chattanooga; Councilors to the American College of Radiology, Walter Hankins, M.D., Johnson City, and alternate, J. Marsh Frère, M.D., Chattanooga.

RADIOLOGICAL HEALTH TRAINING

The United States Public Health Service has announced three courses in radiological health training of particular interest to medical personnel and x-ray technicians, to be held at the Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio.

The courses are:

Medical Aspects of Radiological Health, Nov. 30-Dec. 11, 1959, which is designed primarily for medical, dental, and biological personnel of health agencies who have not had radiological health training.

Radiological Health for X-Ray Technicians, July 6-July 10, 1959, a basic course on the fundamentals of x-ray protection.

X-Ray Protection, Oct. 19-Oct. 23, 1959, a more advanced course for health department, industrial, and institutional personnel responsible for protection in x-ray installations.

Other course dates will be announced later.

For application or further information, write to the Robert A. Taft Sanitary Engineering Center, 4676 Columbia Parkway, Cincinnati 26, Ohio.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

RADIATION BIOLOGY AND CANCER: A COLLECTION OF PAPERS PRESENTED AT THE TWELFTH ANNUAL

SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH, 1958. A volume of 494 pages, with numerous figures and tables. Published for the University of Texas M. D. Anderson Hospital and Tumor Institute by the University of Texas Press, Austin, 1959. Price \$8.50.

GENETICS, RADIobiology AND RADIology PROCEEDINGS, MID-WESTERN CONFERENCE. [Edited by] WENDELL G. SCOTT, M.D., Chairman; Chairman, Committee on Radiology, National Research Council, and TITUS EVANS, Ph.D., Co-Chairman; Member, Committee on Radiology, National Research Council. A volume of 150 pages with figures. Published by Charles C Thomas, Springfield, Ill., 1959. Price \$5.50.

BRONCHOGRAPHY. By C. DIJKSTRA, M.D., Medical Superintendent of "De Klokkenberg," sanatorium and chest hospital, Breda, the Netherlands. A monograph of 158 pages, with 106 figures. Published by Charles C Thomas, Springfield, Ill., 1958. Price \$9.50.

PATIENT CARE AND SPECIAL PROCEDURES IN X-RAY TECHNOLOGY. By CAROL HOCKING VENNES, R.N., B.S., Formerly Surgical Supervisor and Clinical Instructor, University of Minnesota Hospitals, Minneapolis, Minnesota, and JOHN C. WATSON, R.T., Director of Courses in X-Ray Technology, University of Minnesota Hospitals, Minneapolis, Minnesota. A volume of 204 pages, with 62 figures. Published by the C. V. Mosby Company, St. Louis, Mo., 1959. Price \$5.75.

CANCER OF THE SKIN. By JOHN C. BELISARIO, C.B.E., E.D., M.D., Ch.M., D.D.M., Lecturer in Dermatology, the University of Sydney; Senior Honorary Physician for Diseases of the Skin and Member of the Board of Directors, Royal Prince Alfred Hospital, Sydney; Honorary Physician for Diseases of the Skin to the New South Wales Masonic Hospital. A volume of 336 pages, with 201 black and white figures and 8 color plates. Published by Butterworth & Co. (Publishers) Ltd., 88 Kingsway, London, W.C. 2, England, 1959. Price \$10.00.

PREMIER COLLOQUE INTERNATIONAL DE PHOTOGRAPHIE CORPUSCULAIRE, STRASBOURG, 1^{er} AU 6 JUILLET 1957. Colloques internationaux du Centre national de la recherche scientifique, LXXIX. A volume of 452 pages, with numerous figures and tables. Published by Centre national de la recherche scientifique, 13, Quai Anatole-France, Paris (VII^e), France, 1958.

LEHRBUCH DER STRAHLENHEILKUNDE: BEHANDLUNG MIT RÖNTGENSTRÄHLEN UND RADIOAKTIVEN SUBSTANZEN. By RENÉ DU MÉSNIL DE ROCHEMONT, o. ö. Professor für Medizinische Strahlenkunde und Direktor der Strahlenklinik und -Poliklinik der Universität Marburg. With the assistance of Dr. H. J. FIEBELKORN, Prof. Dr. E. H. GRAUL, and Doz. Dr. E. SCHERER, Oberärzte der Klinik. A volume of 764 pages, with 266 figures, including 5 color plates, and 18 tables. Published by Ferdinand Enke Verlag, Hasenbergsteige 3, (14 a) Stuttgart-W, Germany, 1958. Price DM 113.—, paper-bound; DM 119.—, cloth-bound.

Book Reviews

RADIOGRAPHIC ATLAS OF SKELETAL DEVELOPMENT OF THE HAND AND WRIST. By WILLIAM WALTER GREULICH, Professor of Anatomy, Stanford University School of Medicine, and S. IDELL PYLE, Research Associate, Departments of Anatomy, Western Reserve University and Stanford University Schools of Medicine. A volume of 256 pages, with numerous figures and tables. Published by Stanford University Press, Stanford, California, 2d ed., 1959. Price \$15.00.

The second edition of Greulich and Pyle's classic

work on bone age as indicated by the hand and wrist is in essence a complete revision. It is printed on paper of improved quality on which the radiographs and many line drawings are reproduced to better advantage than in the earlier edition. While the main feature is the Atlas, which can be used for quick reference in day-to-day work, the real value of the book lies in the complete academic approach to the problem of bone maturation in the hand and wrist. The outline of maturity factors in the text, with line drawings, brings out details not possible to appreciate on casual inspection of the radiographs. This and the presentation of the material in bold print and the good quality of the reproductions combine to produce an outstanding book.

More space is given to some of the general aspects of body development than in the original work, with elaboration of some pathologic states. Comments are made on the bone changes incident to the Hiroshima bombing, which one of the authors (W.W.G.) has studied in some detail. The text on the applicability and accuracy of skeletal assessment is well worth reading, and the book is a must for the pediatrician as well as his radiologic colleague.

To repeat, this is a revision of a classic, enhanced in value by additional information and charts and improved in its physical aspects by the superior quality of the paper conducive to more satisfactory reproduction of the illustrative roentgenograms.



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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Dynamic Encephalography: A Report of Two Years' Experiences. E. Palma, R. J. Rodriguez Martinez, J. Rodriguez Juanotena, H. Pollero, W. Taibo, F. Gomez Gotuzzo, and W. Perillo. *Acta radiol.* 50: 27-33, July-August 1958. (Montevideo, Uruguay)

In 135 cases a method of encephalography has been used in which oxygen is injected into the cisterna magna above the occipital foramen. Approximately 5 to 10 ml. of cerebrospinal fluid are removed and double that volume of oxygen is injected rapidly. One or more films are obtained as the gas is moving upward. This factor and their practice of allowing any increase in pressure to be equalized by having gas or fluid subsequently leak out through the open needle have prompted the authors to speak of this as "dynamic" encephalography. Additional films are of course made as required by the case.

The method appears most useful in the diagnosis of pathologic processes in the posterior fossa and of expanding lesions of the diencephalon, brain stem, and hypophysis. It is well tolerated and simple to perform. The only contraindication is severe hypertension, especially when there is any danger of tentorial herniation. The removal of fluid takes place in the cisterna magna above the occipital foramen and the risk of herniation of the tonsils in this bony ring is thus avoided.

Three roentgenograms; 1 diagram.

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Lateral Midline Laminography in Encephalography and Ventriculography. Fred C. Shipps and John Raaf. *Am. J. Roentgenol.* 80: 98-103, July 1958. (214 Medical-Dental Bldg., Portland 5, Ore.)

According to the authors, routine performance of laminography is useful in eliminating undesirable superimposed shadows in visualization of the midline ventricular system. The aqueduct of Sylvius, the fourth ventricle, and the third ventricle can be evaluated. The procedure is particularly applicable when a posterior fossa lesion is suspected.

The presence of an indistinct inferior margin in these areas is due to residual fluid. It is therefore recommended that the part of interest be elevated during exposure. Thus, for the aditus of the aqueduct, the brow and vertex should be closer to the table than the chin and occiput.

In 24 cases in which pneumoencephalography or ventriculography had been done, lateral midline laminograms were obtained. Results were graded as adequate or not adequate in reference to visualization of the third ventricle, aqueduct, and fourth ventricle. In pneumoencephalography good filling of the ventricles did not always result in good roentgenograms because of superimposed air shadows in the temporal horns, cisterna ambiens, and cortical subarachnoid spaces. Frequently the ear produced a false shadow of the aqueduct and floor of the fourth ventricle.

Some of the statistics in the text of this article are confusing, since they are not represented in the table of results. The table seems to indicate that lateral

midline laminography succeeds best in visualization of the fourth ventricle (20 cases out of the 24), less well for the aqueduct (17 cases) and least for the third ventricle (16 cases). It is superior, however, to conventional roentgenography for all three areas, the ratio of adequate visualization for the two procedures being 16/9 for the third ventricle; 17/4 for the aqueduct; and 20/9 for the fourth ventricle.

The authors suggest that if there is moderate ventricular filling and the fourth ventricle is not shown by laminography, a cerebellar or brain-stem lesion may be suspected.

Eleven roentgenograms; 1 diagram; 1 table.

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The Use of Pneumoencephalography in the Diagnosis of Headache and Epilepsy. M. Guest and D. P. Jones. *Canad. M. A. J.* 79: 170-172, Aug. 1, 1958. (University of British Columbia, Vancouver, B. C.)

Air encephalograms obtained in 175 cases of epilepsy or headache were studied in an attempt to assess their practical value. In 114 of these cases neither clinical signs, skull roentgenograms, nor cerebrospinal fluid studies showed any abnormality. In 1 of this group a mass lesion was indicated by pneumoencephalography, an infiltrating astrocytoma. In the 61 cases in which clinical signs, skull films, or spinal fluid examination pointed to an abnormality, 16 brain tumors were demonstrated.

Since only 1 brain tumor not otherwise suggested was discovered on pneumoencephalography in a total of 114 patients, and since plain skull films have proved useful in this respect, the authors conclude:

"We ourselves would rarely undertake pneumoencephalography in a patient with normal physical signs; and very rarely if normal signs were supported by the finding of a centrally placed pineal gland. We think the disadvantages of the test may then, in the aggregate, outweigh its benefits. The problem has been well stated by Robertson: 'It may be said that investigation should only be undertaken if there is hope of material help in the conduct of a case, and then it should not be avoided.'" [Robertson, E. G.: *Pneumoencephalography*. Oxford, Blackwell Scientific Publications, 1957.]

Two tables.

A Suggestion for Diminishing the Amount of Gas Introduced into the Subdural Space During Lumbar Pneumoencephalography. Bernard S. Epstein and Joseph A. Epstein. *Am. J. Roentgenol.* 80: 95-97, July 1958. (270 76th Ave., New Hyde Park, Long Island, N. Y.)

The authors have found the following technic helpful in diminishing the handicaps incident to subdural instillation of gas during lumbar pneumoencephalography: After the lumbar puncture needle is introduced into the 4th or 5th lumbar interspace, 10 to 20 c.c. of gas is instilled. Scout roentgenograms are then made and viewed immediately. If the subtentorial or subdural space is visualized, the needle is reinserted at least two interspaces higher, 10 to 20 c.c. of gas is again instilled, scout roentgenograms are again ob-

tained, and the examination is continued if air is in the ventricular system. If a diagnostic lumbar tap has been done within one week preceding the pneumoencephalomyelographic study, the repeat puncture is made two interspaces above the original site.

Six roentgenograms. D. D. ROSENFELD, M.D.
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Arteriographic Demonstration of Collateral Circulation in Cerebrovascular Disease. Gerard M. Lehrer. *Neurology* 8: 27-32, January 1958. (Mount Sinai Hospital, New York 29, N. Y.)

Although the existence of collateral systems in the cerebral circulation other than the circle of Willis has long been known, their functional significance in maintaining the blood supply to the brain in thrombotic or embolic occlusion of the major arterial trunks is not entirely clear. Only relatively recently have reports of sporadic arteriographic demonstration of such collateral pathways in the living patient found their way into the literature. Essentially two types of anastomotic systems have been described (1) between the branches of the three major cerebral arteries on the surface of the brain (see, e.g., Rosegay and Welch: *J. Neurosurg.* 11: 363, 1954. Abst. in *Radiology* 64: 756, 1955), and (2) between branches of the external carotid and ophthalmic arteries (see, e.g., Sachs: *J. Neurosurg.* 11: 405, 1954. Abst. in *Radiology* 64: 757, 1955).

The author reports 3 cases with major vascular occlusions in which such shunts could be clearly visualized in serial carotid arteriograms. In 1 case the functional existence of pial anastomoses between the anterior and middle cerebral arteries was shown, and in 2 anastomotic pathways were demonstrated between the external and internal carotid systems. The clinical picture in these cases and those from the literature appears to indicate that the collateral pathways form an important contribution to the cerebral blood supply. The number of well documented cases recorded to date, however, is not sufficiently large to permit any conclusions as to the prognostic or clinical significance of the demonstrability of collateral circulation by arteriographic means.

Seventeen roentgenograms.

Pneumographic Findings in Angiomata of the Brain. D. L. McRae and V. Valentino. *Acta radiol.* 50: 18-26, July-August 1958. (Montreal Neurological Institute, Montreal, Quebec, Canada)

While angiography is undoubtedly the more reliable method for diagnosing intracranial angioma, this diagnosis may not be suspected and pneumography may be done instead. This paper is based on 35 cases which were examined by pneumography. In only 2 were the findings entirely normal. The changes noted were as follows:

Signs of focal or generalized atrophy.....	12
Combined signs of space-occupying and atrophic lesions.....	7
Interference with the cerebrospinal fluid circulation.....	6
Space-occupying lesions:	
Without intracranial hemorrhage.....	3
With intracranial hemorrhage.....	3
Abnormality of the subarachnoid sulci.....	2

In general the central angioma tend to interfere with the cerebrospinal fluid circulation and obstructive

hydrocephalus is fairly common. In cortical angioma the commonest pneumographic features are those connected with atrophy of the adjacent brain.

Thirteen roentgenograms.

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Radiological Aspects of Cerebellar Astrocytomas and Medulloblastomas. D. L. McRae and Arthur W. Elliott. *Acta radiol.* 50: 52-66, July-August 1958. (Montreal Neurological Institute, Montreal, Quebec, Canada)

The authors collected 200 cases of cerebellar tumors seen at the Montreal Neurological Institute between 1934 and 1955 but deal principally with 50 astrocytomas and 54 medulloblastomas in the age group from birth to fifteen years. Their findings are well summarized in their conclusions:

"Cerebellar tumors in children from birth to age 15 years are usually astrocytomas or medulloblastomas. The only other lesions that may be confused with these are ependymomas, ependymoblastomas, papillomas of the choroid plexus and subarachnoid cysts, but these are exceedingly rare. In posterior fossa dermoid cysts and in cerebellar abscesses there are usually characteristic changes in the bone or in the mastoids which will remove these lesions from consideration."

"In the differentiation of cerebellar astrocytomas and medulloblastomas the following points are of some importance.

"Normal skull films favor the diagnosis of medulloblastoma.

"Skull changes due to chronic increase in intracranial pressure, and especially enlargement of the skull, favor the diagnosis of astrocytoma.

"Calcification of the tumor favors the diagnosis of astrocytoma.

"Demonstration of an intraventricular tumor mass with an irregular surface favors medulloblastoma.

"Extreme enlargement of the lateral ventricles favors astrocytoma."

Twelve roentgenograms; 2 diagrams; 3 tables.

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Clinical Features of Porencephaly: A Review of Thirty-Two Cases. Richard W. Naef. *Arch. Neurol. & Psychiat.* 80: 133-147, August 1958. (Jefferson Medical College, Philadelphia, Penna.)

Porencephaly is defined by the author as a defect in the cerebrum communicating with the ventricles and/or the subarachnoid space, due to a developmental or destructive lesion. The series of 32 cases reported here all occurred prior to, incidental to, or shortly after birth. In 17 patients the lesion presumably occurred during intra-uterine life; 7 sustained a birth injury and 1 a postnatal head injury; in 7 cases the cause was not known. Five cases occurred in premature infants.

In 25 patients the initial symptoms appeared in the first decade, 4 showed symptoms at birth, and 11 others in the first year. The earliest diagnosis was made at the age of six months; the most delayed at the age of fifty. The symptomatology is generally mild in the early years, becoming progressively more severe. It is generally quite manifest in adolescence or early adult life.

In 27 cases the chief complaint was of seizures. In

29 there were signs indicative of focal unilateral cerebral lesions. Spastic weakness with hyperactive reflex changes was present in 25 (bilateral in 2); delayed unilateral limb growth in 14; unilateral sensory disturbance consistent with a parietal lesion in 11; homonymous visual field defects in 7. Mental retardation was evident in 19 patients.

The skull roentgenograms of only 8 patients showed bony abnormalities (such as rarefaction or thinning of the parietal bone), corresponding in all instances with the porencephalic lesion as later demonstrated. Pneumoencephalography was done in all cases and revealed the defect in all but 1. Arteriography was performed in 4 patients, but no significant information concerning the arteriographic appearances in this disease was obtained.

Seventeen roentgenograms; 10 tables.

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Encephalotrigeminal Angiomatosis (Sturge-Weber Disease). Clinical Study of Thirty-Five Cases. Albert F. Peterman, Alvin B. Hayles, Malcolm B. Dockerty, and J. Grafton Love. *J.A.M.A.* 167: 2169-2176, Aug. 30, 1958. (Mayo Clinic, Rochester, Minn.).

Encephalotrigeminal angioma is a congenital disorder, consisting in a venous angioma of the leptomeninges over the cerebral cortex, usually, but not always, associated with a similar vascular lesion (port-wine nevus) over the skin of the face in the area supplied by the trigeminal nerve. Commonly associated clinical findings include convulsive disorders, contralateral hemiplegia, and mental retardation, due to degeneration of the cerebral cortex underlying the meningeal angioma. Less frequent findings include angioma of the choroid, glaucoma, and ipsilateral buphthalmos.

Thirty-five cases treated at the Mayo Clinic over two decades are reviewed. The disease ordinarily presents prominent manifestations in the first few years of life but occasionally medical attention is not sought until the second or third decade. In this series approximately two-thirds of the patients had abnormal skull roentgenograms. Intracranial convolutional calcification, the characteristic roentgen feature, was present in 22 cases, invariably located in the parietal or occipital region. It has been shown that the calcification is in the brain cortex and not in the walls of the angioma as frequently thought (Krabbe: *Arch. Neurol. & Psychiat.* 32: 737, 1934). It may not be evident early in life and may even be absent in some adults. This is held to support the contention of Lichtenstein (Arch. Neurol. & Psychiat. 71: 291, 1954. Abst. in *Radiology* 64: 130, 1955) that the calcification is caused by diminution of the cerebral blood supply and that this result of interference by the vascular malformation causes the sclerosis and atrophy of the brain parenchyma also, but that if these changes occur early in life the obstruction to the flow of blood may become complete so that there is little chance for deposition of calcium in the tissue.

Angiography was done in 5 patients in the present series but revealed no evidence of a vascular lesion. Other authors have reported abnormal findings in approximately half of the cases so studied. Five pneumoencephalograms were obtained, all showing atrophy of the cerebral cortex on the affected side.

Approximately one-half of the patients in this series were able to lead a reasonably comfortable life with the

help of anticonvulsive medication. Patients showing ineffective control of seizures by medical means and in whom mental deterioration is not too advanced may occasionally be benefited by surgical resection of the vascular lesion and damaged underlying cortical areas. Four cases in which craniotomy was performed are reported in moderate detail; benefit was obtained in 2.

The roentgenographic reproductions are small and not very helpful in demonstrating the intracranial calcifications.

Five roentgenograms; 8 photomicrographs; 1 photograph.

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Neuroradiological Findings in Mongolism. K. H. Schiffer, K. Hartung, and H. Strubel. *Acta radiol.* 50: 190-195, July-August 1958. (In German) (Universität von Mainz, Germany)

The authors discuss a group of cases of mongolism presenting hypoplasia of the diencephalon. This circumscribed cerebral hypoplasia corresponds to an area compatible with a deformity of the central part of the base of the skull. This is probably due to an interference with the normal flattening out movement in the development of the base of the skull.

Four roentgenograms; 4 photographs; 1 drawing.

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Thrombolysis with Fibrinolysin in Cerebral Arterial Occlusion. Bernard J. Sussman and Thomas S. P. Fitch. *J.A.M.A.* 167: 1705-1709, Aug. 2, 1958. (Muhlenberg Hospital, Plainfield, N. J.)

The authors report their observation on 3 cases of hemiplegia treated by slow intravenous infusion of fibrinolysin. The site of cerebral vascular occlusion was demonstrated by arteriography in all 3 cases. In one, restitution of circulation in the middle cerebral artery was radiographically demonstrated eight days after beginning of treatment. Clinical improvement was good. In a second patient partial clearing of the occluded carotid lumen was observed, while in the third there was no alteration of the cerebral artery occlusion. The authors believe that prompt administration of fibrinolysin in cases of cerebral thrombosis may prove beneficial.

There were no untoward reactions to angiography in this group of patients. Although the authors are not enthusiastic about the repeated performance of arteriography in cerebrovascular disease, they observed no complications in this group or in another previously reported (Feiring and Sussman, *Neurology* 6: 529, 1956. Abst. in *Radiology* 68: 884, 1957). There is, unfortunately, no alternative to arteriography before and after treatment.

Seven roentgenograms.

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Third Ventricle of 12 mm Width or More: A Preliminary Report. Arne Engeset and Arve Lönnum. *Acta radiol.* 50: 5-11, July-August 1958. (University Hospital, Oslo, Norway)

According to earlier work by the authors "marked enlargement of the third ventricle and the anterior part of the lateral ventricle seemed to indicate a serious clinical condition." In order further to evaluate this possibility they chose 100 patients, without tumor or increased intracranial pressure, in whom the third ventricle had a width of 12 mm. or more. This rela-

tively large measurement was chosen to avoid cases representing a normal variation. (In an analysis of 203 successive encephalographic studies they found that the average width of the third ventricle varied from just over 6 mm. in the six- to fifteen-year-old group to approximately 11 mm. in the fifty-six- to seventy-five-year group.)

The degree of incapacity for work was used as an indicator of the patient's condition. Eighty-eight per cent had completely lost their working capacity, and that ability in the remainder was greatly reduced. The main cause of incapacity was psychic disturbances but disturbances of consciousness, gait, co-ordination, and motility also played a role. The assumption that enlargement of the third ventricle and the anterior part of the lateral ventricle is reflected in the clinical condition was thus supported.

Three figures; 4 tables.

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The Lenticulo-Striate Arteries and Their Diagnostic Value; a Preliminary Report. Poul E. Andersen. *Acta radiol.* 50: 84-91, July-August 1958. (Odense Amts Og Bys Sygehus, Odense, Denmark)

The lenticulostriate arteries are a series of fine vessels which supply the basal ganglia. They usually arise from a region 13 to 15 mm. in length in the upper and posterior part of the middle cerebral artery, on an average between 17 and 30 mm. from the midplane of the skull. In the anteroposterior view they are seen to pass upward medial to the ascending part of the middle cerebral artery. The upper part of the course is fan-like, with the arteries spreading toward the convex floor of the lateral ventricle and the caudate nucleus.

The author was struck by the lack of attention paid to these vessels and set out to evaluate them in a series of 300 successive carotid angiograms. The lenticulostriate arteries were found to be particularly helpful in the diagnosis of atrophic conditions. In the anteroposterior view, when the distance from the most medial of the arteries to the midplane of the skull is more than one-third the distance from that plane to the inner lamina atrophy is probably present. The arteries were also found to be of localizing value in intracerebral tumors and intracerebral hematomas in the internal capsule or arising from ruptured angiomas.

The vessels are more difficult to see in elderly subjects and will be obscured in any patient if the slightest motion occurs.

Four roentgenograms; 5 diagrams; 1 table.

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Neuromuscular and Functional Disorders of the Pharynx. J. P. Murray. *J. Fac. Radiologists* 9: 135-141, July 1958. (Sefton General Hospital, Liverpool, England)

The abnormalities of deglutition in various diseases were studied with the aid of anteroposterior and lateral roentgenograms, fluoroscopy with the image intensifier, and cineradiography.

If myasthenia gravis is suspected, repeated swallows may be necessary to demonstrate dysfunction, and it may be shown best with the patient recumbent. Of 15 cases examined, 11 had some abnormality in the oral or pharyngeal stage of swallowing. In the oral stage, which is under the control of voluntary muscle, one

may see hesitancy in starting deglutition, slow and inefficient tongue movements, difficulty in forming a bolus, and delay in clearing the mouth. Pharyngeal stage dysfunction, which is the main disability in bulbar cases, may be manifest as stasis in the pharynx, loss of tone and ballooning of the pharynx, eventual cessation of swallowing, and nasal reflux. The passage of the bolus is midline in myasthenia; in many cases of poliomyelitis it will be deflected to one side. There is never spasm or hypertrophy of the cricopharyngeus, as in other disorders. Hysterical dysphagia may be differentiated by its failure to respond to prostigmin (1.5 mg. subcutaneously, with 1/100 grain of atropine to minimize side effects).

From a radiological point of view, there are four varieties of hysterical dysphagia: (1) that with apparently normal deglutition; (2) that with delayed initiation and hesitant, tremulous movements of the tongue; (3) that with inability to relax the upper constrictors to receive the bolus from the mouth; (4) that with hypertonicity and prominence of the transverse part of the cricopharyngeus. Only after exhaustive efforts have failed to establish an organic basis for dysphagia should it be diagnosed as hysterical.

The transverse belly of the cricopharyngeus acts as a sphincter between the pharynx and esophagus. The author applies the term "pharyngo-esophageal incoordination" to dysfunction of this muscle, which is manifested by hypertrophy or spasm. This may be idiopathic in old people; a similar condition in younger age groups is usually labeled "globus hysterius." Although the cricopharyngeus can produce a small indentation on the posterior wall of the esophagus in normal subjects, abnormal hypertrophy may be seen in instances of lower esophageal disease, including cardiospasm, carcinoma, and hiatus hernia with reflux.

Twenty-three roentgenograms.

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THE CHEST

Chest Radiography of Prematures: A Planned Study of 104 Patients Including Clinico-Pathologic Correlation of the Respiratory Distress Syndrome. William Allen Bauman and Jerome Nadelhaft. *Pediatrics* 21: 813-824, May 1958. (College of Physicians and Surgeons, Columbia University, New York)

Roentgen studies were made of the chests of 104 unselected premature infants in the first seventy-two hours of life. There were clinical signs of dyspnea sufficient to suggest some degree of the respiratory distress syndrome in 19 of the series and roentgen pictures compatible with hyaline membrane disease were obtained in 35. Twenty-five babies died within the first eight days of life and of the 23 in this group who came to necropsy, 10 had hyaline membranes. In 8 of these both respiratory distress and the pulmonary roentgen appearance of bilateral diffuse increased reticulogranularity had been shown during life. In statistical analyses this association is found to be highly significant ($p < 0.006$).

It is believed that the reticulogranular pattern may precede symptoms of respiratory distress if films are made routinely shortly after birth, particularly in the first hour, in a susceptible population.

That several infants with both roentgen and clinical symptoms of respiratory distress survived indicates that

premature babies may recover from the syndrome. Until the diagnosis can be established with greater certainty during life, the possibility of spontaneous recovery must be considered.

Five roentgenograms; 1 photograph; 2 diagrams; 5 tables.

Bronchography with Dionosil. Om. P. Bhardwaj and Chaman Lall Nagrath. Indian J. Radiol. 12: 99-110, August 1958. (Willingdon Hospital, New Delhi, India)

This report concerns a series of 75 bronchograms obtained with Dionosil in 60 patients. Equal numbers were examined with Dionosil Aqueous, Dionosil Oily, and Dionosil Aqueous mixed with Dionosil Powder. The latter combination gave superior results, with no failures. Coughing during and after the examination was less severe.

Dionosil Oily and Dionosil Aqueous each produced 3 unsatisfactory examinations, requiring repetition. Three of the failures were attributed to warming the medium prior to instillation. In 2 cases in which Dionosil Oily was used, atelectasis and pneumonitis developed.

The authors recommended Dionosil over other bronchographic media and stress their good results with the combination of Dionosil Aqueous and Dionosil Powder. They advise careful local anesthesia and intratracheal catheterization, fluoroscopic control for filling, and no pre-warming of the medium.

Seventeen roentgenograms; 3 tables.

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Intrapulmonary Effusions. Harold A. Swanson. Canad. M. A. J. 79: 8-10, July 1, 1958. (Winnipeg General Hospital, Winnipeg, Man., Canada)

Intrapulmonary effusion, also known as subpulmonic effusion and supradiaphragmatic effusion, may be defined as a collection of pleural fluid between the lung base above and the diaphragm below. It appears with the same contour as the latter and must be distinguished from diaphragmatic elevation due to such conditions as subphrenic infection, phrenic nerve paralysis, eventration of the diaphragm, atelectasis, intrapleural and intrapulmonary neoplastic diseases, diaphragmatic rupture with herniation of a viscous, hepatomegaly, and neoplasms.

The author recently observed 7 such effusions. Two were due to metastatic pleural involvement, 1 was a chylous effusion, and 4 were serous collections associated with heart failure. Blood is frequently found in the subpulmonic space, and pus and other exudates and transudates have been mentioned in the literature.

Small effusions may be present with no discernible abnormality on the ordinary chest film. If physical findings suggest fluid, however, a lateral decubitus chest film should be obtained. For this, the patient lies on one or the other side and a horizontal x-ray beam is directed in a postero-anterior projection through the chest. As the amount of fluid becomes larger, there is pseudo-elevation of the diaphragm, and the increased intrapulmonary effusions are themselves typical in appearance in the usual upright postero-anterior chest roentgenogram. Left-sided subpulmonic effusions are easily detected as a rule, since the distance between the gas bubble in the stomach and the upper surface of the fluid simulating the diaphragm is greater than the dis-

tance between the bubble and the upper surface of a normal diaphragm. The presence of an effusion can also be discovered by observing fluoroscopically the fluid waves produced by the beating heart.

Four roentgenograms.

Caplan's Syndrome: A Perplexing Pneumoconiosis with Rheumatoid Arthritis. Milton Kantor and Charles S. Morrow. Am. Rev. Tuberc. 78: 274-281, August 1958. (VA Hospital, Wilkes-Barre, Penna.)

Caplan described unusual pulmonary lesions in patients with anthracosilicosis who also had rheumatoid arthritis (Thorax 8: 29, 1953). Roentgenographically these were demonstrable as multiple clearly defined rounded densities varying from 0.5 to 5 cm. in diameter scattered throughout both lungs against a background in which other evidence of pneumoconiosis was usually minimal. These densities tended to appear in "crops" and developed rapidly as compared to the conglomerate nodules seen in the usual third-stage silicosis. They appeared before, during, and after the changes of rheumatoid arthritis and tended to be rather stable. They either remained unchanged, underwent calcification, or contracted to leave very small scars. Occasionally they broke down into cavities, which later closed.

The present paper reports a case in a 64-year-old male with third-stage silicosis who had roentgen evidence of pneumoconiosis nine years before admission. His chest showed distinct changes, with formation of rounded opacities of various sizes, which resembled multiple nodular pulmonary metastases. He had clinical manifestations of rheumatoid arthritis seven years before his present admission, with documented conglomerate silicosis prior to the development of the arthritic symptoms. Two of the pulmonary nodules were very large, while the others ranged from 1 to 3 cm. in diameter. No evidence of tuberculosis could be demonstrated.

The authors reviewed 100 patients with silicosis and 35 with silicotuberculosis, all without rheumatoid arthritis. None of them showed pulmonary lesions similar to those described by Caplan. A series of 183 cases of rheumatoid arthritis were also reviewed. This last group included 15 patients with anthracosilicosis, but in none of these was the Caplan type of lesion demonstrated.

The combination of the rare type of pulmonary lesion described with rheumatoid arthritis is designated "Caplan's syndrome." The pulmonary lesions may appear, however, in patients with silicosis in the absence of arthritis. From the roentgenographic standpoint, the chief differential diagnostic consideration is nodular pulmonary metastasis.

Two roentgenograms.

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"Dry" Bronchiectasis. Daniel A. Gillis and R. Drew Miller. J.A.M.A. 167: 1714-1718, Aug. 2, 1958. (Mayo Clinic, Rochester, Minn.)

Bronchiectasis is usually accompanied by a chronic cough with purulent sputum and occasional hemoptysis. When neither sputum nor blood is produced, the bronchiectasis is called dry. The authors review 22 cases of this latter type encountered at the Mayo Clinic in three years. This total represents about 3 per cent of patients found to have bronchiectasis during the same period.

Thirteen patients had previously had one or more epi-

sodes of hemoptysis. Two patients had occasional unproductive cough. Seven had no pulmonary symptoms whatever.

Normal chest films were obtained in 7 cases, while the remaining 15 showed positive changes that ranged from a minimal increase in bronchovascular markings to changes suggestive of bronchiectasis. Bronchograms showed bronchiectasis in all patients, mostly in the right middle and both lower lobes.

Bronchoscopy revealed no abnormalities in 8 patients, but disclosed bleeding in 5, bronchitis in 6, and distortion of the bronchial tree in 3.

Three cases are reported, and the literature is reviewed.

Five roentgenograms.

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Primary Repair of Fracture of the Left Main-Stem Bronchus. Billie G. Streete and Fred E. Stull, Jr. *J. Thoracic Surg.* **36:** 76-80, July 1958. (7100th USAF Hospital, Wiesbaden, Germany)

A case is reported of a fracture of the left main-stem bronchus due to crushing trauma of the chest, with transmission of the force of injury to the closed hollow viscera. The patient experienced no broken ribs or hemoptysis. An immediate expansion of the left lung by closed-tube drainage in this case, followed by complete atelectasis the next day, is attributed to entrance of adjacent mediastinal tissue into the fracture site, causing complete stenosis. Planigraphy and bronchography supplemented bronchoscopy to demonstrate the site and length of the injury. Pleural reaction began increasing rapidly six days after the accident, to produce a massive effusion with shift of the mediastinum to the right, and repeated thoracentesis was required. It was thought that if drainage of the left lung could not be established promptly, pulmonary function and even the lung itself would be lost, due to bronchiectasis or abscess; also that the fractured superior border of the left main bronchus would continue as the source of mediastinitis and effusion.

Repair of the bronchus was carried out twenty days following injury. A year after surgery bronchography showed indentation of the upper border of the bronchus at the cartilage defect, but without a stricture, as noted at bronchoscopy. Vital capacity was 95 per cent of normal, and maximum breathing capacity was 101 per cent of normal.

The recommended treatment of fracture of a main-stem bronchus is re-establishment of continuity as soon as clinically possible so as to prevent bronchiectasis or abscess, with resultant loss of pulmonary functions.

Nine roentgenograms.

Muco-Epidermoid Tumors of the Bronchus Arising from Surface Epithelium. Ronald C. Sniffen, Lamar Soutter, and Laurence L. Robbins. *Am. J. Path.* **34:** 671-683, July-August 1958. (Massachusetts General Hospital, Boston 14, Mass.)

In a study of bronchial adenomas of the carcinoid and cylindromatous types (*J. Thoracic Surg.* **28:** 412, 1954. *Abst. in Radiology* **65:** 292, 1955), 5 tumors were encountered closely resembling these adenomas in behavior and gross appearance, but differing in microscopic structure. The authors briefly outline the clinical and roentgen findings in the 5 patients, with notes on the pathologic observations, treatment, and course.

The symptoms in the 5 patients were quite similar

and were characteristic of slowly developing bronchial obstruction; they were usually intermittent and often absent for long periods of time. The commonest complaints were chronic productive cough, wheezing, and hemoptysis, and the illness was punctuated by episodes of acute pneumonitis. Occasionally there were dyspnea and chest pain. The longest history was thirty years, with repeated episodes of hemoptysis; the shortest was three months, heralded by a bout of pneumonia. The average age at onset of symptoms was forty-five years, the youngest patient being twenty-eight and the oldest sixty-six; at the time of diagnosis and treatment, the average age had risen to fifty-six years, with a range from forty-three to sixty-six years. On physical examination there were no signs except those of pneumonitis to suggest a bronchial tumor.

The roentgen features were of considerable importance in the determination of the presence of a tumor, its localization, and the evaluation of its resectability. In those patients in whom serial roentgenograms were made, one of the most striking aspects was the leisurely growth of the tumors. The principal observations were those indicative of bronchial obstruction or increase in the size of a mass. The slowly growing tumor, as viewed roentgenographically, was roughly spherical or slightly lobulated, and homogeneous in density. It resembled a peripheral primary carcinoma or isolated metastatic neoplasm. No lymph node involvement was demonstrated.

All patients were subjected to bronchoscopy. Although all of the tumors arose in major bronchi (3 in the right upper lobe, 1 in the right lower lobe, 1 in the right main bronchus), 2 were not seen at the time of initial examination.

The microscopic picture in the 5 tumors was sufficiently similar to allow a composite description with the addition of individual variations. The tumors were composed of a series of anastomosing cellular columns and masses separated by thin sheaths of delicate connective tissue. The epithelium in contact with these septa was supported on a distinct basement membrane. In this position the cells were cylindrical and pseudostratified with clearly visible cytoplasmic membranes; the nuclei lay at different levels within adjacent cells. Further from the basement membrane, forming the core of the column, was a mosaic of polygonal cells with poorly defined cytoplasmic membranes. In general, the epithelial cytoplasm was eosinophilic and finely granular. The nuclei of the columnar cells were elongated and lay at right angles to the basement membrane, while nuclei of the polygonal cells were round or ovoid. The chromatin appeared as fine granules and large nucleoli were frequently present. No intercellular bridges or ciliated cells were found.

The clinical courses, roentgen studies, and gross and microscopic structure of the tumors all suggest that they are relatively benign neoplasms comparable in activity to carcinoid adenomas of the bronchus.

Two roentgenograms: 8 photomicrographs; 1 photograph.

Angiocardiography: An Aid for the Early Diagnosis of Bronchogenic Carcinoma. Harold A. Lyons and Franco Vertova. *Am. J. M. Sc.* **236:** 147-155, August 1958. (State University of New York Downstate Medical Center, Brooklyn, N. Y.)

Sometimes angiographic findings may be the first and only diagnostic signs of primary cancer of the

lung. An almost pathognomonic appearance may be demonstrated by angiocardiography and lead to proper diagnosis when all other procedures have been negative or equivocal. Characteristic findings are an interruption to the flow of the contrast material in one of the segmental arteries. Abrupt occlusion and irregularity of the involved artery with absence of distal opacification are the usual findings. Other lesions of the lung or mediastinum may produce occlusion or displacement of a pulmonary artery but the irregular, abrupt termination seen in primary carcinoma is distinctive.

A brief summary of work by previous writers is given and comments are made on characteristic findings at angiocardiography in nonmalignant diseases of the lung.

Three illustrative cases are presented.

The authors conclude that angiocardiography is an important diagnostic aid in bronchogenic carcinoma, particularly when the lesion is peripheral and when other studies have been inconclusive. In their experience this examination has been so fruitful that it has been made a routine procedure in patients with unresolved diagnosis when exploratory thoracotomy is strongly considered. It is noted that a completely normal arterial tree does not exclude malignant disease but that a distorted, stenotic, or occluded branch of a pulmonary artery is nearly pathognomonic of primary carcinoma.

Five roentgenograms. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Diffuse Malignant Mesothelioma of the Pleura. Max A. Forse and Walter A. Haug. Am. Rev. Tuberc. **78**: 268-273, August 1958. (VA Hospital, Portland, Ore.)

This is a case report of a 40-year-old white male with malignant mesothelioma who survived slightly less than one year following the onset of chest pain. At the time of the initial examination he had a pleural effusion on the left. Later roentgenograms showed pleural thickening on the left side and to a lesser extent on the right. Pleural biopsy revealed this to be malignant and at autopsy it was found to represent a malignant mesothelioma. The roentgenogram of the chest taken three weeks before death showed thick soft-tissue density surrounding the left lung, which had the appearance of thickened pleura. On the right the change was much less extensive.

One roentgenogram; 2 photomicrographs; 2 photographs. JOHN H. JUHL, M.D.
University of Wisconsin

Lung Changes in Acquired Heart Disease. Peter Kerley. Am. J. Roentgenol. **80**: 256-263, August 1958. (Westminster Hospital, London, England)

In the acquired heart diseases, the lung changes are most important in mitral valvular lesions and left heart failure. There are six roentgenologic changes in the lungs in mitral valvular disease. The primary ones are (1) distention of veins, (2) distention of lymphatics, and (3) distention and contraction of arteries. Secondary changes include (4) hemosiderosis, (5) bone formation in the lungs, and (6) pulmonary fibrosis, secondary emphysema, and atelectasis.

Under normal circumstances, the upper lobe veins on the roentgenogram are invisible or nearly invisible while the lower lobe veins, particularly on the right, are quite easy to identify. With mitral stenosis, the elevated left atrial pressure is at once transmitted to the

pulmonary veins so that the upper lobe veins become prominent radiographically. This change takes place early and perhaps before there is any clinical evidence of a valvular lesion and shortly after the phase of acute endocarditis. As the mitral stenosis becomes established, the upper lobe veins remain distended and the lower lobe veins become invisible. If the disease process results in fibrous ankylosis of the valve and incompetence occurs, the distended upper lobe veins will gradually disappear (unless left ventricular weakness supervenes).

The author feels that these hemodynamic changes are dramatic roentgenologic manifestations of mitral stenosis. As the venous pressure rises above the plasma osmotic pressure, there is a transudation of fluid and the pulmonary lymphatics become visible as transverse lines at the bases. In acute episodes, the deeper lymphatics also become visible as long straight lines varying from 2 to 5 inches in length. The intercommunicating lymphatics, which are seen first, are shown as shorter horizontal streaks seldom more than 1 inch in length. Visualization of the deep lymphatics is usually transient while visualization of the intercommunicating lymphatics may vary little. Congested lacteals may also be seen in acute or chronic left ventricular failure and in some forms of malignant disease and pneumoconiosis.

Changes in the pulmonary arteries are also manifested roentgenographically. In minor degrees of mitral stenosis, there is little or no alteration. In more severe degrees of pulmonary hypertension, the main pulmonary artery and the right and left branches and second-degree branches are enlarged, while the peripheral branches are narrowed and tortuous. These changes occur gradually; simultaneously the venous distention and lymphatic engorgement appear to become less obvious as vasoconstriction becomes more severe and cardiac output is reduced. Therefore, the lung fields may appear to be hypertranslucent when the patient is clinically terminal. Reduced pulmonary vascularity should, of course, arouse suspicion of an associated pulmonary stenosis and this must be excluded clinically when such radiographic features are demonstrated.

Summarizing the findings, the author states that distended upper lobe veins and contracted lower lobe veins in the presence of visible lymphatic lines indicate that mitral stenosis is dominant over mitral insufficiency. Distended upper lobe veins plus interstitial lines and small peripheral arteries indicate predominant stenosis with pulmonary hypertension. Distended upper and lower lobe veins indicate a low pulmonary pressure. Perhaps it is even feasible to grade the mitral lesion by these patterns.

Of the secondary pulmonary manifestations of mitral valvular disease, hemosiderosis is the most common. Bone formation in the lungs is almost conclusive evidence of mitral stenosis and is believed to occur in 3 to 5 per cent of patients with this disease. There may be multiple calcified opacities scattered widely through both bases. Late pulmonary changes also occur in the bases in the form of fibrosis, fibrous thickening of the pleura and emphysema, perhaps associated with atelectasis. Many patients experience more disability from these secondary pulmonary sequelae than they do from the mitral deformity.

Unusual complications of mitral stenosis are pulmonary artery and pulmonary vein thrombosis. In

either instance, the diagnosis may be suggested by the local area of increased pulmonary radiability. In thrombosis of a pulmonary vein, there should be an associated local area of congested lymphatics and angiography may actually demonstrate the thrombus.

The radiographic manifestations of left ventricular failure include distention of upper lobe veins, lymphatic swelling and edematous lymph nodes in the hilar regions, slight interstitial edema with transverse lines at the bases and occasionally lamellar pleural effusions. In a certain percentage of cases, some combination of these signs appears before any clinical evidence of failure. For example, prominence of the upper lobe veins may occur prior to clinical manifestations of decompensation and is an indication that the patient is on the verge of failure.

Eleven roentgenograms. JOHN W. WILSON, M.D. Johnstown, Penna.

Eventration of the Diaphragm: Herniation of the Liver into the Left and Right Hemithorax. A Case Report. Moses Grossman, Rita Brady, and H. Brodie Stephens. *J. Thoracic Surg.* **36**: 120-125, July 1958. (University of California Medical Center, San Francisco 22, Calif.)

The authors present a case of eventration of the diaphragm in a boy of five and a half years. The only abdominal organ extending into the chest was the liver, which occupied the right as well as the left chest. No previously recorded cases of bilateral eventration of the diaphragm could be found in the literature.

The patient was admitted to the hospital because of deformity of the thorax, poor growth, and a "mass in the chest." Roentgen examination revealed a large homogeneous mass in the lower anterior portion of the thorax which was contiguous with the contour of the anteromedian segment of both the right and left hemidiaphragm as well as the base of the cardiac silhouette. Fluoroscopy showed no abnormality of diaphragmatic excursion. The mass, which moved synchronously with both leaves of the diaphragm, exhibited no alteration in size or shape with respiration and no intrinsic pulsation was detected. Angiocardiography disclosed no abnormality of the cardiac chambers or of their sequence of opacification. The cardiac silhouette, however, was compressed and displaced cephalad and slightly posterior by the large mass, in which no contrast material was detected. Although the study did not conclusively establish the location of the mass, a tentative diagnosis of mediastinal tumor—most probably a pericardial cyst—was made.

Bilateral exploratory thoracotomy and limited laparotomy were performed. What was found appeared to be a failure of development of the tendinous portion of both hemidiaphragms, involving the central tendon of the diaphragm only. The liver protruded through this central portion of the diaphragm and presented itself in the chest just posterior to the lower segment of the sternum. It was located in the midline immediately beneath the heart and had a bilobular appearance. Repair of the very large defect was considered impossible.

The roentgen findings associated with partial eventration of the right leaf of the diaphragm with herniation of the liver are usually sufficiently characteristic that the diagnosis can be made with ease. In the present case, however, the location of the mass immediately inferior to the heart and centrally in the chest was misleading.

To the authors' knowledge eventration of the diaphragm in this particular location has not been recorded previously. Angiocardiography was performed to ascertain further the relation of the anteromedian mass to the heart and to the diaphragm. This clearly revealed that the mass was extracardiac, but did not clarify its position with respect to the diaphragm. In retrospect, it is apparent that pneumoperitoneum would have led to the proper diagnosis preoperatively.

Five roentgenograms; 2 photographs.

THE CARDIOVASCULAR SYSTEM

Diseases of the Heart and Great Vessels: Thoracic Roentgenographic Manifestations. André J. Bruwer, Corrin H. Hodgson, and John A. Callahan. *Am. J. Roentgenol.* **80**: 264-296, August 1958. (Mayo Clinic, Rochester, Minn.)

Congenital and acquired diseases of the heart and great vessels frequently mimic primary pulmonary or mediastinal diseases. The authors include a long list of chest abnormalities that may give rise to these confusing pulmonary manifestations, grouping them in the broader categories of (1) pulmonary entities, (2) pleural entities, (3) entities of the bony thorax, and (4) mediastinal manifestations of cardiovascular disease.

(1) **Pulmonary Entities:** *Vascular congestion* in cardiac failure may result in generalized exaggeration of the pulmonary vascular markings; basal edema tending to obscure the diaphragmatic outline; pleural effusion; and scattered areas of irregular consolidation. These findings could be confused, for example, with basilar bronchiectasis. They are usually transient and reversible under medical treatment.

In vascular congestion in left-to-right shunts, notably in septal defects and patent ductus arteriosus, there is an increased pulmonary vascular volume, but the radiographic appearance differs from that in congestion related to cardiac failure. The vessels are prominent and are easily identified. Even when failure is superimposed and a characteristic haziness is added to the roentgen picture, the appearance usually remains distinct from that in cases of acquired or degenerative heart disease. If the volume of the left-to-right shunt is overwhelming, patches of pulmonary consolidation may be seen.

Lymphatic congestion, occurring particularly in mitral valvular heart disease, is reflected in the appearance of costophrenic septal lines (Kerley's B lines). The hilar lymph nodes may also become enlarged as a result of lymphatic engorgement in mitral stenosis.

Pulmonary hemosiderosis and *pulmonary ossification* in the form of multiple disseminated calcific lesions of the lung are other manifestations of mitral stenosis.

Pulmonary embolism and infarction may be manifestations of several types of cardiac disease but particularly myocardial infarction and bacterial endocarditis. The roentgen picture varies and x-ray diagnosis is subject to considerable error.

Pulmonary edema with the characteristic "bat-wing" or "angel-wing" configuration is also listed under the pulmonary entities. It is noted that acute pulmonary edema may manifest itself unilaterally.

Decreased pulmonary vascularity may be encountered, usually in the tetralogy of Fallot, pure pulmonic stenosis, Ebstein's malformation of the tricuspid valve, or tricuspid atresia.

Enlargement of the bronchial arteries may occur as a

result of obstruction of the pulmonary arteries and presents roentgenographically as irregular branching pathways unlike the normal orderly branching of pulmonary arteries.

An anomalous venous connection of the right lower lung is to be suspected when an anomalous vessel is seen in the right lower lung field following a course toward the inferior vena cava. Laminography and angiography may corroborate this diagnosis. Partial agenesis of the right lung is occasionally associated.

Intralobar bronchopulmonary sequestration presents as a solid or cystic lesion in the posterior basilar segment of the lung receiving its arterial supply from an anomalous vessel arising from the aorta.

Pulmonary arteriovenous fistula is frequently one feature of a familial disease known as hereditary hemorrhagic telangiectasia or Rendu-Osler-Weber disease. Radiographically it is seen as a lobulated mass in any part of the lung with visible afferent and efferent vessels. Fluoroscopically the pulmonary mass can be shown to vary in size with the Valsalva and Müller maneuvers.

(2) *Pleural Entities: Pleural effusion* is commonly associated with heart disease and failure. The effusion occurs more commonly on the right side; occasionally it may loculate in the interlobar fissure and present on the postero-anterior roentgenogram as an oval mass. The lateral view will identify the interlobar location of the mass and indicate its etiology. These effusions disappear promptly with medical treatment. Effusions may also loculate in the mediastinal reflection of the pleural cavity, giving rise to a distorted mediastinal silhouette or simulating the appearance of a collapsed lobe, or they may collect in the infrapulmonary space and simulate elevation of the diaphragmatic leaf. Decubitus views provide a prompt differential diagnosis.

(3) *Entities of the Bony Thorax:* Notching of the ribs due to coarctation of the aorta is perhaps one of the best known roentgenologic manifestations of cardiovascular disease. Intercostal arteriovenous malformations may also give rise to localized notching of a rib. Aneurysm of the innominate artery is usually associated with aneurysmal formation at the arch of the aorta and may cause characteristic erosion of the medial end of the clavicle or manubrium. Aneurysms of the ascending or descending limbs of the aortic arch may cause painful erosions of the sternum or dorsal vertebrae, respectively.

(4) *Mediastinal manifestations of cardiovascular disease* are divided into those conditions that affect the aorta and its brachiocephalic branches, conditions affecting the pulmonary artery, conditions affecting the thoracic veins, and conditions affecting the heart and pericardium.

Conditions affecting the aorta and its brachiocephalic branches include: coarctation of the aorta, manifested by alterations in the contour of the aortic knob and descending aortic limb; congenital kinking of the aortic arch, which may be mistaken for a mediastinal mass or coarctation of the aorta; a right-sided aortic arch; dextroposition of the descending aorta; aneurysms of the sinus of Valsalva, which may present as masses beyond the heart border either to the right or left; aneurysms of the thoracic aorta (including traumatic aortic aneurysms), which may simulate mediastinal tumors; aneurysms and buckling of the innominate and carotid arteries; anomalous right subclavian artery, arising as the last branch of the

aortic arch, passing behind the esophagus or between the trachea and esophagus into the right upper extremity, and producing anterior deviation of the trachea that can be seen on a routine lateral view of the chest; simple tortuosity of the descending thoracic aorta producing pressure on the esophagus.

Conditions affecting the pulmonary artery that may be reflected in the chest roentgenogram are: poststenotic dilatation of the pulmonary artery in pure pulmonary stenosis; absence of a pulmonary artery, which is associated with reduction in the size of the lung and hemithorax on the involved side, reduction in the pulmonary vascular markings, and perhaps a lace-like pattern of bronchial arteries; aneurysmal dilatation of the pulmonary artery; an anomalous course of the left pulmonary artery, anterior and to the right of the lower trachea and over the right main stem bronchus before passing behind the trachea to the left lung.

Conditions affecting the thoracic veins include a total anomalous pulmonary venous connection, a left superior vena cava, anomalous course of the azygos vein or dilatation of the normal azygos vein, each of which conditions may be reflected in alterations of the mediastinal or, in the case of the last, right hilar shadows.

Of conditions affecting the heart and pericardium, mention is made of Kartagener's triad of dextrocardia, bronchiectasis, and sinusitis; calcified myocardial infarcts; ventricular aneurysm, which may simulate a mass adjacent to the apex of the heart; pericardial celiomes and diverticula.

Eighty-two roentgenograms; 2 photographs; 2 diagrams.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Pericarditis with Effusion: New Observations, with a Note on Ewart's Sign. Israel Steinberg. Ann. Int. Med. 49: 428-437, August 1958. (525 E. 68th St., New York 21, N. Y.)

The author demonstrates by angiography that pericardial effusions begin in the infracardiac diaphragmatic portion of the pericardium. As fluid increases, the retrosternal pericardial space is filled.

In pericardial effusions, the heart is surrounded by fluid, except posteriorly, where pericardial reflections over the inferior vena cava below and the pulmonary veins, pulmonary artery, and aorta above prevent accumulation of fluid. Because of the retrosternal pericardial accumulation, the blood-filled cardiovascular structures are forced backward, compress the lung and bronchi, and produce the so-called Ewart's sign. This sign, described by Ewart in 1896, consists in an area of variable size with dullness in the region of the inferior angle of the left scapula, associated with a corresponding area of bronchial breathing, and increased fremitus and egophony. Ewart attributed it to partial collapse of pulmonary tissue and pressure on a bronchus.

In massive pericardial effusions, marked distention of the lateral pericardial pouches occurs; they behave like inflated water wings and cause additional compression, enhancing Ewart's sign. Pericardial paracentesis through the posterior approach, when made low in the thorax, yields fluid either from the infracardiac pericardial space or from the lateral pericardial pouches. To avoid traversing lung, the anterior route in the region of the xiphoid process or apex of the heart is recommended for paracentesis.

Nine roentgenograms. HARRY HAUSER, M.D.
Cleveland Metropolitan General Hospital

Conditions Permitting Regurgitation of Radiopaque Contrast Material Through the Intact Mitral Valve. Herbert M. Stauffer and Morton J. Oppenheimer. *Am. J. Roentgenol.* **80:** 253-255, August 1958. (Temple University Hospital and School of Medicine, Philadelphia 40, Penna.)

Regurgitation of a radiopaque contrast medium through a normal mitral valve has been demonstrated experimentally in dogs, by means of cineradiography. This regurgitation occurred in situations during which the phase of diastasis in the cardiac cycle is increased, as in bradycardia, sinus arrhythmia, temporary asystole, and the compensatory pause following a premature contraction. Since these interruptions in the cardiac cycle may occur in patients during left ventricular angiography, the differentiation of "physiologic regurgitation" and pathologic regurgitation becomes extremely important.

In the study reported here, also in dogs, conventional roentgen techniques were used to demonstrate regurgitation through a normal mitral valve, occurring during vagal asystole (long diastasis). Simultaneous electrocardiographic records were obtained. These are essential to show whether any arrhythmias exist and may be correlated with the roentgen exposures to determine whether a simultaneous mitral regurgitation was obtained, thus differentiating physiologic regurgitation from cardiac insufficiency.

Four roentgenograms; 1 electrocardiogram.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Corrected Transposition of the Great Vessels Associated with Intracardiac Defects. Burton W. Fink, Forrest H. Adams, Russell A. McFall, and Bernard J. O'Loughlin. *Pediatrics* **21:** 381-387, March 1958. (F. H. A., Department of Pediatrics, U.C.L.A. Medical Center, Los Angeles 24, Calif.)

"Corrected transposition of the great vessels" is defined as an embryologic error of unknown etiology in which the heart has the gross appearance of complete transposition of the great vessels but the functional capacity of a normal heart. Four patients have been seen at the Medical Center Hospital of the University of California (Los Angeles) in whom this diagnosis was made on the basis of evidence obtained from cardiac catheterization and angiography. The diagnosis was confirmed by surgery in 1 patient and by surgery and necropsy in another. Because of the similarity of the cases, only 1 is presented in detail and the significant data from the other 3 are summarized.

Corrected transposition of the great vessels can occur as an isolated asymptomatic lesion. More frequently inversion of the ventricular loop and failure of retroversion of the proximal truncus, which are believed to be contributing factors, tend to leave additional defects. Three of the authors' patients had interventricular defects; 1 of these also had a patent ductus arteriosus associated with the primary defect.

Roentgen examination disclosed symmetrical enlargement of the heart. Electrocardiography consistently showed evidence of right ventricular hypertrophy. Cardiac catheterization and angiography were the most informative of all the studies. Because of the position of the great vessels, attempts to introduce the cardiac catheter into the pulmonary artery were often unsuccessful. In those instances in which the pulmonary artery could be entered, the catheter was observed

to be abnormally displaced in a medial direction. Angiocardiography was especially helpful in establishing the correct anatomic diagnosis. With good concentration of the contrast medium and simultaneous lateral and anteroposterior roentgenograms, the relative positions of the pulmonary artery and aorta were accurately defined.

A fifth case of corrected transposition of the great vessels is mentioned in an addendum.

Six roentgenograms; 6 drawings; 3 tables.

Persistence of Fetal Ductus Function After Birth: The Ductus Arteriosus as an Avenue of Escape. Herbert L. Abrams. *Circulation* **18:** 206-226, August 1958. (Stanford University School of Medicine, San Francisco 15, Calif.)

In fetal life there is a veno-arterial shunt by way of the ductus arteriosus, presumably because the unexpanded fetal lungs offer too high a resistance to the flow of blood through the pulmonary arteries. It is therefore reasonable to expect that, if a lesion is present which increases significantly the pressure in the pulmonary system, the ductus will remain open and continue to shunt blood from the right ventricle into the aorta.

The author presents well authenticated examples of all but one (congenital mitral stenosis) of the interesting array of conditions which can cause persistent right-to-left flow in a patent ductus. The list starts with pulmonary hypertension caused by increased arteriolar (pulmonary) resistance. Next is atelectasis and/or agenesis of the pulmonary parenchyma [capillary?], then occlusion of the common pulmonary vein. Mitral atresia, mitral stenosis, aortic atresia, aortic stenosis, and finally coarctation proximal to the ductus complete the list.

It is well known that when the ductus is serving as "an avenue of escape" because of increased resistance, ligation is usually fatal. The author points out that in the one group listed above that is generally amenable to surgery, namely, coarctation, the pulmonary hypertension which occurs is analogous to that seen in adults with left ventricular failure from any cause, and is similarly reversible if the cause of the left-sided failure (in this case, the coarctation) can be corrected.

The examples are well illustrated and diagrammed. Nineteen roentgenograms; 12 diagrams; 2 tables.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Roentgen Diagnosis of Acute and Chronic Traumatic Aneurysm of the Thoracic Aorta. Israel Steinberg and John A. Evans. *Am. J. Roentgenol.* **80:** 237-247, August 1958. (525 E. 68th St., New York 21, N. Y.)

Rupture of the thoracic aorta due to blunt trauma occurs most frequently just beyond the point of fixation by the brachiocephalic arteries and insertion of the ligamentum arteriosum. This was found to be the most common site in a series of 72 cases reported by Strassmann (Am. Heart J. **33:** 508, 1947), while 20 per cent occurred in the ascending aorta just above the cusps and another 20 per cent in the descending aorta between the isthmus and diaphragm. In most cases the aortic rupture was through-and-through, in which event fatal hemorrhage usually results. Rupture may be incomplete, the adventitia being preserved and dissected away from the medial layer, with formation of an interposing thrombus, which eventually is enveloped

by a connective tissue wall, forming a false aneurysm. Only patients with incomplete rupture survive.

Patients who have experienced blunt thoracic injuries should be followed by periodic roentgenograms of the chest. The initial finding radiographically is a widening of the mediastinum and obscuration of the arch owing to the formation of a mediastinal hematoma. This may be associated with hemothorax on the left. The hematoma may subside, but within two to four weeks a prominence in the region of the aortic knob may become evident. Usually within two months an aortic mass is obvious and subsequently the outline of an aortic aneurysm becomes distinct. Calcium may be deposited in older aneurysms. Fluoroscopically the aneurysm may or may not be pulsatile depending upon whether a thrombus has formed. The typical location of the aneurysm in the aorta can be demonstrated by angiography in the left anterior oblique view.

The authors present a summary of 4 cases of traumatic aneurysm of the aorta that were found incidentally in asymptomatic patients on routine roentgenographic surveys of the chest.

Clinically, aneurysms of the thoracic aorta following blunt trauma are divided into acute and chronic types. The acute type may be associated with unconsciousness, shock, multiple fractures, and internal injuries which divert attention from the thorax and consideration of aortic rupture. Chronic aneurysms may be asymptomatic or may produce dyspnea, cough, and pain in the chest.

In the differential diagnosis, syphilitic aneurysms, arteriosclerotic aneurysms and congenital anomalies of the aorta associated with kinking and dilatation of the left subclavian artery (pseudocoarctation) must be considered. In the acute stage, aortic rupture may simulate a mediastinal tumor. Mediastinal hematomas also result from bleeding of neighboring vessels, particularly venous channels.

Chronic traumatic thoracic aortic aneurysms may be treated by resection and homografts. This surgical procedure is considered formidable and thus a careful selection of cases is necessary. Aneurysms that produce symptoms may be assumed to be enlarging and should be resected. Even in the absence of symptoms enlargement of an aneurysm is an indication of persistent bleeding, a prime indication for surgery.

Twenty-four roentgenograms; 1 diagram.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Calcification of the Ascending Aorta. A. Elkeles. *Brit. J. Radiol.* 31: 420-423, August 1958. (Prince of Wales's General Hospital, London, N. 15, England)

Calcification of the intima of the ascending aorta has been recognized by radiologists as a valuable sign of syphilitic aortitis. Similar calcification observed in roentgenograms of nonsyphilitic cases is believed to be rare. The author examined chest films of 256 patients with proved syphilis, ranging in age from twenty-one to eighty-one years. The earliest age at which calcification of the ascending aorta could be demonstrated was forty-five years. There were 173 patients in this series over forty-five, and 22 (13 per cent) of this age group showed calcification. Only 8 cases of calcification of the ascending aorta in nonsyphilitic cases were observed by the author during the interval (1949-1957) in which the syphilitic patients were studied.

Calcification of the ascending aorta in older individu-

als with no clinical or serological evidence of syphilis is probably due to arteriosclerosis, especially when calcifications are also present in the descending and abdominal aorta. In syphilitic aortitis, calcification is usually confined to the ascending aorta, appearing as a thin line along the lateral aortic wall. The calcifications in arteriosclerosis, when they are present in the ascending aorta, are dense and occur in the vicinity of the coronary ostia and posterior medial wall (Lodwick and Gladstone: *Radiology* 69: 70, 1957). Syphilitic aortitis apparently predisposes to the formation of atherosomatous plaques in the otherwise relatively immune ascending aorta.

Five roentgenograms.

SAMUEL B. HAVESEN, M.D.
University of California S. F.

Abnormal Mediastinal Shadows Caused by the Tortuous Thoracic Aorta. Itaru Ohara and Aiichi Tanno. *Am. J. Roentgenol.* 80: 231-236, August 1958. (Tohoku University Hospital, Sendai, Japan)

The tortuosity and elongation of the thoracic aorta commonly seen in older persons can ordinarily be easily recognized as a cause of mediastinal shadows. Occasionally, however, the shadows may be confusing and may closely mimic mediastinal tumors. Three short case histories are presented in which dilatation and elongation of the thoracic aorta caused rounded mediastinal shadows suggesting a diagnosis of tumor.

The true nature of the shadows can usually be determined by additional simple roentgen studies including overpenetrated films, fluoroscopy with barium swallow, and oblique views. Angiocardiography and/or laminography may be useful.

In each of the cases reported the descending aorta crossed over the vertebral column to the right side at the base of the chest so that the descending aorta formed part of the right heart border or presented as an independent shadow to the right of the spine.

Seven roentgenograms; 3 drawings.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Azygos Vein Dilatation Simulating Mediastinal Tumor. W. H. Shuford and H. S. Weens. *Am. J. Roentgenol.* 80: 225-230, August 1958 (Emory University, Atlanta 3, Ga.)

The authors report the case of a man of forty-nine years with thrombosis of the inferior vena cava and cardiac decompensation, with subsequent azygos vein dilatation of such degree as to simulate a mediastinal tumor. Plain films of the chest obtained shortly after hospital admission revealed a discrete spherical mass, 3 cm. in diameter, in the right tracheobronchial angle in the anatomic region of the azygos vein. There was little change in the size of the shadow with change in position or intrathoracic pressure. Ten days after admission, however, it had decreased significantly in diameter. Intraosseous venography was performed by injection of Diodrast into the transverse process of D-11 and the nature of the mass was established by its opacification. As the patient's condition improved and cardiac compensation was regained, the vein decreased in size, returning almost to the normally invisible state.

The anatomy of the azygos system is briefly reviewed. In the presence of faulty development or obstruction of the inferior vena cava, the azygos system may afford one of the main routes by which venous cir-

culation is maintained. Rarely, however, has dilatation of the azygos vein reached such proportions as to suggest a mediastinal tumor. The authors believe that in their case cardiac decompensation was an important factor. In 6 clinically normal persons in whom inferior vena cava ligation had been performed one to ten years earlier, no increase in the size of the azygos shadow was observed.

When a mass in the region of the azygos vein is demonstrated radiologically, fluoroscopic examination and roentgenograms in various positions and with changes in intrathoracic pressure may give a valuable clue to the nature of the shadow. If it is the result of a dilated azygos vein, these maneuvers will ordinarily change its size [though this was not true of the authors' case].

Seven roentgenograms; 1 drawing.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Syndromes Associated with Hypoplasia or Aplasia of One Pulmonary Artery. Bernard F. Vaughan. J. Fac. Radiologists 9: 161-168, July 1958. (Royal Perth Hospital, Perth, Western Australia)

The different conditions in which undervascularization of one lung is a common factor are discussed, with illustrative case reports and comments from the literature.

In congenital absence of a pulmonary artery the affected lung is smaller, with a crowded bronchial tree and usually some shift of the mediastinum. Because of cardiac rotation, absence of the usual hilar densities may not be appreciated. The bronchial arteries become engorged, and left ventricular output is increased. If the heart is normal, it is usually the right pulmonary artery that is absent. Hemoptysis may occur from hemorrhage due to the high pressure in the bronchial arteries, and there may be a decreased exercise tolerance. Angiocardiography confirms the diagnosis. It is postulated that alveoli are expanded by an erectile effect owing to the pressure of blood in their capillaries; if this effect operates throughout life, it would explain the decrease in size of a lung which is seen in both congenital and acquired obstruction of a pulmonary artery.

Absence of the left pulmonary artery may be associated with the tetralogy of Fallot. The patient is cyanotic and the affected lung is hypoplastic; however, the opposite lung may show evidence of increased vascularity. Unilateral bronchiectasis can simulate absence of a pulmonary artery roentgenographically. There is diminished vascularity in the affected lung, decrease in size of its artery, and possibly some increase in the bronchial arteries. Bronchography confirms the diagnosis. Unilateral emphysema may also produce this picture, but it has been argued that in these cases the primary abnormality is hypoplasia of a pulmonary or lobar artery.

A case of pulmonary artery obstruction due to carcinoma of the bronchus is presented; there was no mass or atelectasis on the roentgenograms, the primary sign being a considerable decrease in the circulation of one lung! A case of atrial septal defect with a hypoplastic left lung and pulmonary artery is also reported.

Nineteen roentgenograms

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Results of Anatomical and Pathological Studies on the Carotid Artery After Percutaneous Punctures of the

Vessel and Its Clinical Significance. A. Rimpau and H. Seils. *Acta radiol.* 50: 77-83, July-August 1958. (In German) (Allgemeine Krankenhaus Heidelberg, Hamburg, Germany)

Hamburg, Germany)

The authors examined more than 200 cases after carotid artery puncture and present the anatomical and histologic findings in this large material. In about 99 per cent of the cases there was evidence of penetration of the needle through the walls of the carotid so that an entrance and exit opening was noted. In about 8 per cent of cases a hematoma in the wall was seen. The significance of this occurrence is emphasized and it is pointed out with a conclusion that if a hematoma is sufficiently large it will inevitably lead to occlusion of the lumen. When gross bleeding was encountered, it was noted that the vena jugularis had been punctured. Complications at the puncture site have been encountered only occasionally, but the authors raise a question whether subsequent deterioration in the clinical condition might not be caused by injury to the wall of the vessel and its occlusion.

Four photomicrographs

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Experimental Coronary Arteriography. Sven Bellman and Howard A. Frank. J. Thoracic Surg. 36:33-43, July 1958. (H. A. F., 300 Brookline Ave., Boston 15, Mass.)

A technic is described for coronary angiography in the surgically exposed heart, with standard radiographic equipment. It has been employed in 18 dogs. The method was not designed primarily for clinical use but to provide a detailed *in vivo* demonstration of the pattern of the left (or the right) coronary artery immediately prior to a direct experimental or surgical procedure upon the coronary vessels. Angiograms of high quality were obtained, and there was little evidence of ill effect.

Single-exposure arteriograms delineated the coronary arterial vessels almost to the limit of naked-eye resolution, *i.e.*, to 0.2 mm. in diameter, as measured in the postmortem specimen. There was little variation in the *in vivo* pattern visualized in repeated angiograms during a single sitting. The only change observed was in branches at the limit of *in vivo* demonstration; this was probably due to cardiac and respiratory motion rather than a true change in vessel diameter.

Comparison of *in vivo* roentgenograms with the more detailed studies in excised hearts gave further confidence in the reliability of the method. The injection of contrast medium in itself did not provoke any change in vascular pattern or lead to the closing or opening of vessels of the size visualized.

Six roentgenograms: 3 photographs

The Subclavian Arteries: Roentgen Study in Health and Disease. Nathan Poker, Nathaniel Finby, and Israel Steinberg. *Am. J. Roentgenol.* 80: 193-216, August 1958. (New York Hospital, New York, N. Y.)

This paper is based upon observations of the subclavian arteries accumulated in twenty years experience with roentgen visualization of the cardiovascular system. Roentgenographically these arteries are invisible in frontal and lateral views. The left subclavian artery can be visualized, however, in a left anterior oblique film of the chest as the anterior margin of the "aortic triangle." Angiographically all of the vascular trunks arising from the aortic arch are demonstrable.

the right subclavian artery being best seen in a frontal projection, and the first part of the left in the left anterior oblique view.

The normal dimensions of the subclavian arteries, as determined by direct film measurement, are presented in a table. The average (approximate) length of the left artery is 5.0 cm., of the right 6.1 cm. The average normal calibers are 16 mm. for the right at its summit and 9 mm. for the left at its midpoint. The subclavian arteries are shortened in arteriosclerotic and hypertensive cardiovascular disease and to a lesser degree in cardiovascular syphilis. Distortion, displacement, and shortening may accompany intrathoracic neoplasms.

A detailed classification of pathological conditions affecting the subclavian arteries is given, and each of these is taken up separately. Included are: congenital anomalies; the thoracic inlet syndrome; buckling of the arteries; aneurysms of various origin; arteriovenous fistulas; occlusion, as in so-called "pulseless disease" (Takayasu disease) and thrombosis; tumor involvement ("Pancoast tumors"); changes referable to congenital interruption of the aortic arch; occlusion incident to the Blalock-Taussig operation; deformity due to thoracoplasty and kyphoscoliosis.

This paper contains a wealth of valuable information to which an abstract cannot do justice. The conditions discussed are beautifully illustrated by selected angiograms and accompanying line drawings. A lengthy bibliography is appended. Those interested in angiography will find this communication well worth detailed study.

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Cheyenne, Wyo.

The Normal Axillary Venogram. C. Jules Rominger. *Am. J. Roentgenol.* 80: 217-224, August 1958. (Misericordia Hospital, Philadelphia 43, Penna.)

The arm veins of 100 presumably normal persons were examined by making a single anteroposterior roentgenogram of the arm and shoulder during the rapid injection of contrast material for routine intravenous urography. The contrast agent used in all studies was 76 per cent Renografin. Films were made with non-Bucky technic with the patient maintaining normal quiet respiration. The antecubital vein and the basilic vein were both found to be satisfactory routes of injection for an axillary venogram, but with injection into the cephalic vein demonstration of the axillary system is frequently poor. The most favorable time for roentgenographic exposure in normal cases appeared to be five to ten seconds after the injection is begun.

Venograms of the right and left arms showed no appreciable differences. There were, however, striking differences in the venous systems of males and females. In the male the arm veins tended to be straighter and of greater diameter, and to have fewer valves and less prominent paravalvular sinuses. Fewer small tributaries were shown and anatomic variations were less frequent. Measurements of the veins at various levels were made directly on the roentgenograms and these values are presented in tabular form.

Characteristics of the venous valves are discussed at some length. These are visualized on venograms as bulges of varying size in the vein outline, depending on the degree of distention of the paravalvular sinuses. When the valves are wide open, the vein presents a smooth, tubular appearance and the valves are not visible. With the valves partly closed, the venous channel is correspondingly narrowed producing a coni-

cal or tapered appearance. With complete closure of the valves, the contrast material shows an abrupt endpoint, concave proximally. The more nearly closed the valve, the larger the proximal paravalvular sinuses tend to be. It was found that maneuvers which increase the intrathoracic pressure (e.g., Valsalva test) will result in venous back pressure and cause the valves to close and the paravalvular sinuses to become prominent.

The valvular images described, sometimes called "images by stenosis" and "images by blocking," have frequently been misconstrued as representing pathological changes. Actually these changes are normal physiologic findings. "The only valid roentgenographic evidence of subclavian vein obstruction is the demonstration of extensive collateral circulation."

The number of valves demonstrable in the axillary vein is usually two in either sex. Three is the average number in the basilic vein and one in the cephalic vein.

Thirteen roentgenograms; 4 tables.

JAMES W. BARBER, M.D.
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Splenoportography: Some Advantages and Disadvantages. Melvin M. Figley. *Am. J. Roentgenol.* 80: 313-323, August 1958. (University Hospital, Ann Arbor, Mich.)

One of the disadvantages of splenoportography is the unpredictability of the results. In 125 attempts on 111 patients there were 21 (16 per cent) outright failures, attributed to the following causes: failure to find the spleen—no injection (4 cases); failure of transport of contrast material or extrasplicenic injection (11); roentgenographic failure (3); unknown (3). Inexperience and the fact that no test injection was used were responsible in some instances. Failure to find the spleen occurred only when it was not palpable.

Another disadvantage is the significant number of suboptimal examinations. Twenty-two of the author's attempts resulted in only fair to poor roentgenograms. Part of these difficulties were due to exceptionally large patients (3) and avoidable roentgenographic error (5), but the bulk were attributable to partial loss of contrast medium by extravasation from the spleen (14). This may be the fault of the "controlled injection technic," since during respiratory motion the needle may become less tightly gripped by the spleen. [By controlled injection we understand localizing the spleen and the puncture site on a preliminary roentgenogram and giving a test injection of contrast medium if necessary.]

The single major hazard of splenoportography is serious post-puncture bleeding, and this fortunately is unusual. Two patients in the author's series were still bleeding at laparotomy thirty to sixty minutes later, and in another 300 to 400 c.c. of blood was found to have accumulated near the spleen.

Two general types of visualization are obtained by splenoportography. One shows only the splenic vein fed by one or more hilar tributaries and the portal vein and its branches. Such changes are regarded as excluding portal obstruction or portal hypertension. The other type, showing sustained hepatofugal flow in portal and splenic tributaries, is considered suggestive of some portal or splenic obstruction. Determination of the site of obstruction, whether intrahepatic or extrahepatic, is one of the principal indications for splenoportography. In 46 patients with liver cirrhosis examined adequately by the author, the vein was found

patent in all but 1. In 9 cases diagnosed as extrahepatic obstruction due to portal vein thrombosis, liver biopsy was normal in all. Thus in a series of 55 cases only 1 was erroneously diagnosed in respect to the site of occlusion.

The second principal use of splenopertigraphy has been to detect expansive processes in the liver, the signs being occlusion and deformity of the portal branches and defects in the hepatogram—that phase of uniform liver density produced by sinusoidal filling. Useful information was obtained in 16 patients with liver disease other than cirrhosis. Two large cysts and 8 "sizable" tumors were detected but disseminated disease with small local lesions caused no alteration except hepatomegaly. On occasion, in an apparently normal liver, opacification is not uniform and defects have been observed where there was no palpable abnormality. Thus, the splenopertigraphic signs of hepatic neoplasm must be regarded in the light of the clinical situation. They are presumptive but not infallible evidence.

The third major use of splenopertigraphy has been in search of evidence of pancreatic neoplasms which may displace or invade the portal or splenic veins. In only 4 of 9 cases of neoplasms of the pancreas (primary or regional involvement) were there convincing signs of tumor. In 3 cases of pancreatic cysts some splenic vein obstruction was noted, twice due to the mass and once due to splenic vein thrombosis related to pancreatitis. Thus it would appear that sizable pancreatic neoplasms may not be recognized, particularly in the head. Further, it appears that benign processes may produce the same nonspecific signs of compression and thrombosis that occur with malignant lesions.

The above study of 125 attempts at percutaneous splenopertigraphy and review of several analyses by others, together totaling nearly 500 examinations, permits the following conclusions.

1. Splenopertigraphy is usually successful with very simple technic, but it carries a certain percentage of failure and substandard opacification.

2. Splenopertigraphy is relatively free of major hazard considering the seriousness of the problem for which it is used. Bleeding requiring transfusion or splenectomy may be expected in about 2 per cent of the patients who undergo the procedure.

3. Splenopertigraphy accurately indicates the presence of portal obstruction. Variations in technic do not influence portal hemodynamics. The site of obstruction is usually but not always identified.

4. Splenopertigraphic alterations due to hepatic and pancreatic neoplasm occur inconstantly. Reliance cannot be placed on a negative examination.

Fifteen roentgenograms; 2 tables.

HEINRICH B. WASMUTH, M.D.
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Percutaneous Splenic Portography in Amebic Liver Abscess. Tawan Surawongse Bunnag, Virul Kaoparisuthi, Sillawat Arthachinta, Kalaya Chienpradit, and Luang Binbakaya. *Am. J. Roentgenol.* **80:** 324-329, August 1958. (Chulalongkorn Hospital, Bangkok, Thailand)

A study of 26 cases of liver abscess was undertaken (1) to demonstrate the intrahepatic portal venous pattern in this disease, (2) to locate the abscess for the clinician, and (3) for follow-up after specific therapy. The positive diagnostic signs were: (1) an enlarged liver with proportional increase in the diameter and length

of the portal veins, which at the same time retained their smooth curves and gradual tapering caliber, as long as cirrhosis did not intervene; (2) hypertrophy of healthy liver tissue, most often the left lobe, probably compensatory; (3) an avascular area in the liver; (4) absence of delay in liver opacification (since there was no increased intrahepatic pressure, the sinusoids were opacified in six to nine seconds); (5) absence of reflux or varices, except when cirrhosis was also present.

The site of abscess in the liver can be determined due to the fact that only the undamaged blood vessels are opacified, fewer vessels appear in the roentgenographic field, and these show less superimposition than those of the normal hepatogram.

A number of cases are described and illustrated. Thirteen roentgenograms; 1 table.

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The Anatomy of Collateral Circulation. Edward A. Edwards. *Surg., Gynec. & Obst.* **107:** 183-194, August 1958. (Peter Bent Brigham Hospital, Boston, Mass.)

In this paper the author has sought to bring angiography and clinical evidence to bear upon our concepts of the morphology and effectiveness of the various collateral circulatory systems. A collateral path is one which bridges an obstruction in a vascular trunk, either arterial or venous. Vessels which may be considered potential collaterals generally follow a course parallel, not transverse, to the obstructed trunk. Branches beyond an obstruction should not be considered collaterals, but should be termed the "distribution system." The circulatory status of the distal tissues depends as much on the patency of this system as on the state of the collateral system.

A second vascular system to an organ, such as the lung, heart, or liver, constitutes a "supplementary" variety of collateral. This system may be unable to maintain the viability of an organ because of differences in pressure and fluid content.

One vessel of an anastomotic system may be larger and more extensive in its distribution than the other vessels. Occlusion of the preponderant artery under these conditions causes more ischemia than occlusion of its smaller partner. Such an unbalanced system is not uncommon in the case of the coronary arteries.

The effectiveness of collateral systems depends on (1) the size of the anastomoses; (2) the occlusion pattern in respect to collateral involvement; (3) functional needs of the tissue supplied; (4) associated spasm of anastomosing vessels and distributing vessels; (5) dilatation of vessels; (6) general factors affecting blood flow and blood content.

In general, because of the multiplicity of veins and their free anastomosis, there is less interference with flow after venous occlusion than after arterial. In some locations, however, valves oppose collateral flow until dilatation makes them incompetent.

Three roentgenograms; 3 diagrams.

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University of Pennsylvania

The Mobile Unit X-ray Survey in Cardiovascular Disease Detection: A Report of 129,894 70 mm. X-rays, 3,477 Referrals. Milton Feig, Donald C. Cameron, and Agnes Jensen. *Wisconsin M. J.* **57:** 261-265, July 1958. (State Board of Health, Madison, Wisc.)

The authors report the cardiovascular findings on

129,894 70-mm. chest x-ray films taken during 1955 by the Wisconsin State Board of Health mobile x-ray units. The study was secondary to the tuberculosis-screening program. In general, the survey method was the same as that reported by Feig and Jensen in 1949-1951 (Wisconsin M. J. 54: 151, February 1955. Abst. in Radiology 66: 129, 1956).

The population surveyed was relatively young, able-bodied, and in good health, as industrial groups were encouraged to participate in the screening program and all films obtained in mental institutions, homes for the aged, and general hospitals were excluded from the study. Children under fifteen years of age are not included in these surveys unless there is definite history of exposure to tuberculosis.

On the basis of the film-readers' impressions, 3,477 persons were referred to their family physicians, who confirmed the presence of heart disease in 1,904 (14.6 per 1,000 studies). Using the terms "old" and "new" to signify heart disease previously known to the screener as opposed to previously unknown or unrecognized disease, 627 cases of "old" heart disease were detected by the survey; this is a rate of 4.8 per 1,000 persons examined. The examination was directly or indirectly responsible for the discovery of "new" disease in 1,277 persons, which represents a rate of 9.8 new cases per 1,000 films. An unexpected finding was that in only 940 (15 per cent) of 6,244 persons who had a positive history of cardiovascular disease were the roentgenograms "suspicious."

Three tables.

THE DIGESTIVE SYSTEM

Leiomyosarcoma of the Esophagus. J. D. Martin, Jr., and Jennings M. Grisamore. *Surg., Gynec. & Obst.* 107: 238-242, August 1958. (Emory University, Atlanta, Ga.)

A case of leiomyosarcoma of the upper one-third of the esophagus in a 75-year-old woman is presented. The patient had experienced progressive dysphagia for two years, with a 70-pound weight loss and, more recently, dyspnea in the recumbent position. Barium swallow revealed dilatation of the upper esophagus with apparent stricture in the midportion; the lesion was missed on esophagoscopy. Superficial biopsy led to a diagnosis of leukoplakia. At operation a pedunculated polyp weighing 9.1 gm. was removed from the upper esophagus, showing the microscopic features of leiomyosarcoma. Nineteen months after operation the patient was doing well; the findings on barium swallow appeared normal but there was a probable metastatic lesion in the right lung.

The 20 cases of leiomyosarcoma previously reported are reviewed. The tumor is of rare occurrence, whereas leiomyoma of the gastrointestinal tract is seen fairly frequently. Diagnosis is confirmed only at operation and biopsy is indicated, since simple resection is adequate for leiomyoma.

The leiomyosarcomas are relatively benign compared to other sarcomas, and even in the presence of local metastases resection to relieve obstruction is justified.

Three roentgenograms; 3 photomicrographs; 1 photograph; 1 table summarizing the cases from the literature.

D. J. RITCHIE, M.D.
University of Pennsylvania

The Significance of Prolapse of the Gastric Mucosa. David E. Dines, Lloyd G. Bartholomew, James C. Cain, and George D. Davis. *Gastroenterology* 35: 166-175, August 1958. (L. G. B., Mayo Clinic, Rochester, Minn.)

In the seven-year period 1948 through 1954 the diagnosis of prolapse of the gastric mucosa was made radiologically in 158 patients at the Mayo Clinic. This represents an incidence of 1 in 1,000 gastrointestinal series. Rigid criteria must be met before a diagnosis of prolapse is made. The pylorus and duodenal bulb must be displayed at a right angle to their longitudinal axis. In this projection one must by palpation or mechanical compression demonstrate fairly parallel rugal folds extending through the pyloric canal and emerging into the base of the duodenal cap. Moreover, this phenomenon must be observed during more than one effective peristaltic wave. There results a filling defect in the barium-filled duodenal bulb. Unless one can demonstrate that the free margin of the radiolucent structure has a wavy uneven contour, he should doubt the presence of true prolapse. Rather he may be viewing invaginating pyloric muscle or a projectional illusion of such.

There were 128 male and 30 female patients in the authors' series. In 63 patients prolapse was the only radiographic abnormality. Of this number, 56 had symptoms referable to the gastrointestinal tract, of which 44 were finally labeled as "functional" in nature. Only 6 patients had "ulcer-like" symptoms. Six others had upper gastrointestinal bleeding.

Ninety-five (60 per cent) patients had associated gastrointestinal conditions. Duodenal ulcer (40 cases) was the most common, but practically the entire gamut of gastrointestinal tract disease was found in association with prolapse.

The authors conclude that prolapse of the gastric mucosa rarely occurs as an isolated finding. It usually accompanies the customary signs of some inflammatory condition of the duodenum or antral portion of the stomach or both.

Eight roentgenograms; 4 tables.

MAJ. MARTIN A. THOMAS, M.C.
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Jejunogastric Intussusception—An Unusual Complication of Gastric Surgery. Bert Bradford, Jr., and James E. Boggs. *Arch. Surg.* 77: 201-204, August 1958. (603 Atlas Bldg., Charleston, W. Va.)

The authors review the literature and report a case of jejunogastric intussusception occurring in a 74-year-old man, seven years following subtotal gastrectomy, successfully diagnosed and treated. Up to 1955 about 100 cases were reported in the world's literature (Irons and Lipkin: *Ann. Surg.* 141: 541, 1955), including only 10 from the United States.

Aleman (Acta radiol. 29: 383, 1948. Abst. in Radiology 52: 757, 1949) divided the cases into three groups: Class I, an intussusception of the afferent loop of the jejunum into the stomach lumen; Class II (75 per cent of the cases) intussusception of the efferent loop; Class III (relatively rare) prolapse of both loops through the gastroenterostomy stoma.

The etiology of the condition is unknown. The clinical picture, while variable, is usually characterized by sudden onset of severe epigastric pain followed by vomiting. Hematemesis may occur. On physical examination, there may be only epigastric tenderness early in the course, but later the abdomen may become

rigid. A palpable mass was noted in about 10 per cent of the reported cases.

Early diagnosis is important, as patients operated on in the first forty-eight hours after onset of symptoms have a mortality rate of 10 per cent, while after forty-eight hours the mortality rises to 54 per cent. The diagnosis is made by barium-meal examination. Aleman considered a striated filling defect in the stomach pathognomonic. A polypoid mass is visible within the stomach, with the base at the site of the gastroenterostomy stoma. The size of the mass varies with the amount of intussuscepted jejunum. Parallel lines, spirals, or concentric circles across the mass represent collection of barium between the valvulae conniventes. There have been no reported cases of recurrence following surgical reduction.

One roentgenogram.

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Gas Cysts of the Intestine (Pneumatosis Intestinalis).
Zuheir Mujahid and John A. Evans. *Surg., Gynec. & Obst.* **107**: 151-160, August 1958. (New York Hospital-Cornell Medical Center, New York, N. Y.)

The clinical, radiological, and pathological features of pneumatosis intestinalis, an uncommon affection of the gastrointestinal tract in man, are reviewed. The first case was reported in 1730 by DuVernois, who discovered it during the dissection of a cadaver. Some 255 cases had appeared in the literature up to 1952 (Koss: *Arch. Path.* **53**: 523, 1952. *Abst. in Radiology* **60**: 619, 1953). [This figure has been augmented by a not inconsiderable number of reports in the last five or six years.—Ed.] The disease is well known to veterinarians, occurring more frequently in the lower animals, particularly pigs.

Pneumatosis intestinalis occurs as an incidental finding and in the absence of associated mechanical complications produces no symptoms. It is often associated with other lesions of the digestive tract, such as gastric and duodenal ulcer. The cysts may occur in the stomach, small or large bowel, or the mesentery. They may be mucosal or submucosal in location and they vary from a few millimeters to several centimeters in diameter. The contained gas is high in nitrogen as well as CO₂ and oxygen.

Pathogenesis is discussed. The most widely accepted theory assumes a break in the mucosa due to intestinal distention; gas is then forced through the mucosal defect into the submucosa or subserosa, forming a cyst-like collection. Others believe that the cysts represent distended lymph spaces, and this theory is supported by their microscopic appearance, which shows an endothelial layer forming the walls. The cysts are surrounded by a nonspecific inflammation which, in all probability, is a foreign body reaction to the presence of gas.

The intestinal cysts have a characteristic radiographic appearance on barium contrast examination, frequently permitting a definitive diagnosis. Roentgen evidence of pneumoperitoneum in a patient without symptoms or signs of a perforated viscus should also lead to consideration of the condition. Air cysts in the mesentery may be suggested on scout films by bizarre, relatively fixed midabdominal gas collections not conforming to the pattern of intestinal gas. Small intestinal and barium studies will show these collections to be outside the intestinal tract. Intramural cysts are

demonstrable as sharply marginated polyp-like defects, with varying degrees of obstruction.

The most common complications are bowel obstruction, perforation with tension pneumoperitoneum, and bacterial invasion of the walls of the bowel which results in a bacterial colitis.

The authors review 7 cases collected from the official records of the New York Hospital.

Seven roentgenograms; 2 photomicrographs; 3 photographs.

MIGUEL CHIAPPORI, M.D.
University of Pennsylvania

Diocetyl Sodium Sulfosuccinate (Doxinate) as an Adjunct in the Roentgenologic Investigation of the Gastrointestinal Tract—A Clinical Study. Angus K. Wilson. *Am. J. Roentgenol.* **80**: 89-94, July 1958. (343 S. Main St., Salt Lake City, Utah)

To overcome dehydration of barium sulphate suspension in the large intestines after oral ingestion, the author uses a fecal softener. The compound, diocetyl sodium sulfosuccinate (DSS), reduces the surface tension between the aqueous and solid constituents of the bowel and results in a soft homogeneous fecal mass. The author gives the patient one 240-mg. capsule of preparation at the time of initial ingestion of barium sulphate suspension. If the patient takes barium suspension several hours before appearing in the Radiologic Department, the capsule is taken along with the barium. Otherwise, it is given immediately upon completion of the fluoroscopic and roentgenographic examination. The compound has been found useful in the examination of 800 patients.

Fifty-one roentgenograms.

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Oral Roentgenology of the Gallbladder. Christian V. Cimmino. *Virginia M. Monthly* **85**: 373-379, July 1958. (Mary Washington Hospital, Fredericksburg, Va.)

The properly executed gallbladder examination is unexcelled in accuracy, especially in regard to the presence of stones. Technic with the patient horizontal and the ray vertical is no longer acceptable.

Gallbladder and gastrointestinal studies should be made at the same time, as a rule, because of the impossibility of a clinical differential diagnosis in certain patients, particularly middle-aged women, and because of the tendency toward coexisting disease in the two systems.

The fatty meal is of limited importance in the gallbladder examination. It should be used (a) in an effort to detect noncalculous filling defects in the infundibulum when the density in this segment is suboptimal because of gravity, and (b) when there is a suspicion of Rokitansky-Aschoff sinuses in the gallbladder with segmental constriction and with poorly defined contours. Determination of the degree of contraction following the fatty meal is of limited value; the diagnosis of "sluggish gallbladder" is unsatisfactory.

Diagnosis of "poor-concentration" can largely be avoided by the additive technic.

All noncalculous filling defects in the gallbladder constitute an adequate indication for surgery, lest a potentially or frankly malignant lesion be missed.

One of the following will constitute the majority of roentgenologic reports of gallbladder studies: normally concentrating gallbladder with or without stones; non-

visualized gallbladder with or without demonstrable stones; suboptimally concentrating gallbladder with stones.

Nineteen roentgenograms; 2 photomicrographs; 2 photographs.

AUTHOR'S SUMMARY

Operative Cholangiography. Eric Samuel and W. Trubshaw. *South African M. J.* 32: 595-598, June 7, 1958. (Johannesburg, Union of South Africa)

A relatively simple and inexpensive apparatus which fulfills the requirements for successful operative cholangiography is described. It consists of a wooden cassette tunnel (6 X 2 feet) exactly the same size as the operating table. The upper surface is made of lead plywood with the exception of a Perspex window. Within the tunnel is a linen runner with six pockets, each 12 inches long, accommodating 12 X 10-inch cassettes; four of these pockets are loaded so that the first lies in position under the Perspex window. The first two pockets in the runner are filled with dummy cassettes. The whole apparatus is placed on the operating table and over it the patient is put in position for surgery.

For injection of the medium into the exposed cystic duct, a polythene tube is used of such a length as to allow the surgeon to stand outside the radiation beam. Films are taken after the injection of 5 ml., 7.5 ml., and 10 ml. of contrast material and a serial study of the differential filling of the ducts is thus made. The catheter is then withdrawn; the films are developed and inspected immediately. If the cystic duct is not available for injection, the bile ducts are filled by inserting directly into the common duct a needle connected via a polythene catheter to the syringe. The flexible tube between the penetrating needle and the syringe enables the surgeon's hands to be well outside the range of radiation and also minimizes the risk of spill of the medium which so often occurs from a fixed needle and syringe.

On an average, cholangiographic study by this method adds five minutes to the operating time.

Four roentgenograms; 3 photographs; 2 drawings.

Opacification of Radiolucent Biliary Calculi. Emanuel Salzman, David H. Watkins, and William R. Rundles. *J. A. M. A.* 167: 1741-1743, Aug. 2, 1958. (Denver General Hospital, Denver, Colo.)

A procedure was recently described whereby radiolucent biliary calculi were identified by their opacification after prolonged Telapaque administration (Salzman and Warden: *Radiology* 71: 85, 1958). The opacified calculi were characterized by the "rim sign," a sharp linear density outlining the periphery of the stone. Opacification of gallstones was found to occur both in the presence and absence of gallbladder visualization. Common-duct stones were opacified in the absence of duct visualization.

A case is now reported in which hepatic and common duct stones were demonstrated, but not the gallstones found at autopsy. *In vitro* studies showed that the opacifying quality is inherent in the stone and is not to be attributed to an instability of the colloid system of the bile.

This technic may be useful in demonstrating calculi in the common bile duct after cholecystectomy.

Six roentgenograms; 8 photographs.

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THE MUSCULOSKELETAL SYSTEM

Massive Osteolysis—Disappearing Bones. G. Blundell Jones, R. L. Midgley, and G. Stewart Smith. *J. Bone & Joint Surg.* 40-B: 494-501, August 1958. (G. B. J., 14 Barnfield Hill, Exeter, England)

Massive osteolysis, or disappearing bones, is a condition of young adults in whom gradual bone resorption develops, unassociated with significant constitutional or blood chemical changes. It may follow minor injury, but it is evidently quite different from the atrophy of disuse. The cause has not yet been definitely determined. Histologically, fibrous tissue of abundant vascularity always seems to be present, and Gorham and Stout (*J. Bone & Joint Surg.* 37-A: 985, 1955, Abst. in *Radiology* 67: 302, 1956) believed that a relationship exists between the hemangiomatous changes and the osteolysis.

The previous literature of 26 such cases is reviewed, and another case is reported. In this patient there was gradual complete disappearance of the left scapula and the outer third of the clavicle, with partial absorption of several ribs, during a five-year period following a doubtful injury to the clavicle. Ultimately a mass of fibrous tissue formed about the thoracic duct, obstructing it, and producing death from chylothorax. Interestingly, a similar termination was observed in one other case previously reported in the literature (Gorham *et al.*: *Am. J. Med.* 17: 674, 1954, Abst. in *Radiology* 65: 474, 1955). Fibrous tissue surrounding the left subclavian vessels examined histologically in the present case showed large anastomosing vascular spaces, such as were described earlier by Gorham and Stout.

[See following abstracts and 2 reports recently appearing in *Radiology* (Johnson and McClure 71: 28, 1958; Hambach *et al.*: 71: 43, 1958).—Ed.]

DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Disappearing Bones. S. M. Milner and S. L. Baker. *J. Bone & Joint Surg.* 40-B: 502-513, August 1958. (13 St. John St., Manchester 3, England)

This is the report of a case in which gradual progressive disappearance of the left humerus, clavicle, and scapula was observed over a ten-year period. The initial complaints, occurring at the age of sixty, followed a fall in which the shoulder and arm were bruised. The first indication of bone absorption became apparent two years later, when radiographs revealed irregular areas of decreased density in the clavicle and scapula. During the next eight years the process progressed inexorably. As of 1958, the upper arm was completely flaccid and flexible. The patient was free from pain. She had control of wrist and finger movements, but with considerable decrease in strength.

At no time in the course of this case was there evidence of bone disappearance or abnormal density in any other part of the skeleton. Very complete clinical laboratory studies were entirely normal. Arteriograms showed no evidence of hemangioma or other pathology.

Histologic sections revealed distention of venous capillaries in the areas of involvement. There was also increased osteoclastic activity out of proportion to the osteoblastic activity. No general vascular congestion of the soft tissues in the region was present.

Seven roentgenograms; 8 photomicrographs; 1 photograph. DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

A Case of "Massive Osteolysis" of the Femur. J. N. Aston. *J. Bone & Joint Surg.* 40-B: 514-518, August 1958. (St. Bartholomew's Hospital, London, E. C. 1, England)

This report describes spontaneous gradual absorption of a large segment of femur in an eighteen-year-old girl. Following the insidious appearance of shallow periosteal erosion in the midshaft region, bony destruction progressed, leading finally to repeated pathological fractures. Application of a bone graft did nothing to stay the course of the disease, and ultimately extraperiosteal resection of the femur was carried out.

Histologically, biopsy tissues and those following resection showed cystic spaces occupied and lined by cavernous or sinusoidal tissue, which appeared to be eroding the adjacent bone. The characteristic vascular tissue present was suggestive of some type of angioma of bone.

This is the condition called "massive osteolysis" by Gorham and Stout (*J. Bone & Joint Surg.* 37-A: 985, 1955. *Abst. in Radiology* 67: 302, 1956) and reported by others as "disappearing bones."

Six roentgenograms; 2 photomicrographs; 2 photographs.

DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Notes on a Rare Case of Essential Osteolysis. Francisco Branco and J. da Silva Horta. *J. Bone & Joint Surg.* 40-B: 519-527, August 1958. (Institute of Oncology, Lisbon, Portugal)

In a 13-year-old boy lymphangitis of the leg developed after a puncture wound of the foot. Intermittent swelling of the thigh ensued. Eleven months after injury the femur fractured spontaneously. Radiographic findings suggested Ewing's sarcoma, and radiation therapy was given. The femur underwent progressive rarefaction and then destruction, which spread centrifugally to involve the knee joint, the right side of the pelvis, and the sacrum. Eventually the absorption crossed to the opposite of the pelvis, so that the pubis and ischium disappeared bilaterally, along with the wing of the ilium on the first affected side, and most of the sacrum. This all took place over a twelve-year period, during which time extensive laboratory studies, tissue studies, and radiographic examinations were carried out.

The authors found no increase in local vascularity on repeated biopsies, and suggest that the hyperemia reported by others in association with massive osteolysis may be secondary to the primary process. However, they found nothing to throw light on the etiology of the disease.

Many types of treatment were tried without benefit, including administration of androgens, calcium fluoride, suprarenal extracts, vitamin D₃, aluminum acetate solution, ultraviolet irradiation, placental extracts, vitamin B₁₂, ionized calcium, somatotrophic hormone, and transfusions of placental blood.

Five roentgenograms; 4 photomicrographs; 1 photograph; 1 diagram; 1 table.

DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Unexplained Destruction of the Shaft of the Femur in a Child. R. W. Butler, R. A. McCance, and A. M. Barrett. *J. Bone & Joint Surg.* 40-B: 487-493, August 1958. (Addenbrooke's Hospital, Cambridge, England)

The authors report the case of a 5-year-old child in

whom, while at play, a fracture occurred in the femoral shaft from negligible trauma. During his treatment by traction in a hospital ward, there was an initial formation of a small amount of callus, which soon reabsorbed. This was followed over a five-month period by absorption and disappearance of the upper two-thirds of the femoral shaft. Radiographic studies were very complete, and full clinical, biochemical, and histological investigations were carried out, but no general or local abnormalities other than the femoral destruction were apparent.

The process appeared to stabilize about nine months after the fracture, and there was some remineralization of the lateral cortex of the femoral shaft during the next nine months. It was finally possible, by surgical application of bone grafts and a rigid bone strut, to restore the femoral shaft to good weight-bearing condition.

No diagnosis has been made. Abundant vascularity of tissue was remotely suggestive of an angiomatic condition. The location seemed to the authors consistent with the theoretical possibility of eosinophilic granuloma. Although histologic findings were not characteristic, there were eosinophils in the connective tissue.

Seven roentgenograms; 4 photomicrographs; 7 diagrams.

DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Osteo-Chondro-Dystrophy Hypercalcemia Idiopathica: An Atypical Case of Morquio's Disease. Andrew Melkis and Hans Mautner. *Arch. Pediat.* 75: 285-289, July 1958. (Pownal, Maine)

The authors report a case of dwarfism with spinal changes typical of Morquio's disease and severe deformities of the long bones and especially of the hip joint. The roentgenograms were evaluated by Dr. Felix G. Fleischner as follows:

"Films of the chest, pelvis, hands, skull, and lumbar spine reveal essentially normally developed skull and chest, except for small size. The skeletal changes are most marked in the lumbar region, where there is flattening of all of the vertebral bodies which are also irregular in contour and exhibit a tendency toward wedging with a central prolongation of the vertebral body anteriorly, forming a so-called tongue. The first lumbar vertebra is markedly wedged and shortened in A. P. diameter. These changes are all typical of those found in Morquio's disease. The femoral heads are quite hypoplastic and irregular in association with large and irregular acetabula. The metacarpals and phalanges are short, with pointing of the bases of the metacarpals and also the distal ends of the proximate phalanges. These changes of the hands and hips are also typical of this entity."

The final diagnosis was Morquio's disease, with some similarity to the Jansen variation, without any suggestion of heredity and with compensatory hyperparathyroidism and an unexplained partial hyperthyroidism.

A Case of Endemic Fluorosis of Bone in the Cape Province. L. Werbeloff and B. Sender. *South African M. J.* 32: 720-723, July 19, 1958. (University of Cape Town, Cape Town, Union of South Africa)

A case of endemic fluorosis of the bones in a 30-year-old Negro woman from South Africa is reported. There were no dental lesions. Diagnosis was based on the clinical features and the x-ray appearance. Essential roentgen features were osteosclerosis and calcification

tion of the ligaments and muscular attachments. In particular, the sacrotuberous and sacrosciatic ligaments were affected.

This condition can be recognized by a progressive rigidity of the trunk in patients who have been exposed to high-fluoride drinking water for approximately twenty years or in those exposed to dust containing fluoride in industrial processes for two and a half to three years.

In the first stage of the disease there are increased bone density and exaggerated trabeculation with medullary narrowing, so that other causes of osteosclerosis have to be differentiated. Once the ligamentous and muscular attachments calcify, the disease enters the second stage, in which the present case falls. In the third stage the trabecular structure is completely hidden by the chalk-like appearance which may extend to the skull and the metacarpals and phalanges, which are usually the last to be affected. Finally, there is complete immobilization of the thorax with abdominal breathing, and the chest becomes barrel-shaped and flattened anteriorly. Spinal cord pressure may result from bony encroachment, with loss of sphincter control.

Because the patient's drinking water may now contain a more normal fluoride content, it remains to be seen what the outcome in her case will be in the next ten years.

Four roentgenograms; 1 photograph.

Osteo-Articular Lesions in Smallpox. K. S. Bose. *J. Indian M. A.* 31: 151-154, Aug. 16, 1958. (Medical College Hospitals, Calcutta, India)

The author reports 12 cases of smallpox with osteoarticular involvement. Nine were in a subacute stage occurring two to six months after desquamation of the scabs and 3 were late cases, seen one to twelve years after the original infection.

The x-ray appearance of bone in the subacute cases resembled chronic pyogenic osteomyelitis but differed in that the ends of the bones forming the joint were affected. Small cystic changes and subperiosteal bone formation without sequestra and without marked necrosis and new bone formation were more or less characteristic. Another important observation was that both epiphysis and metaphysis were involved along with the joints. Joint changes included separation of the joint space, erosion of the articular ends of the bones, and moderate periarticular soft tissue swelling. In late cases, the joint space was diminished with deformed articular ends and unequal growth causing valgus deformity.

Five roentgenograms; 1 photomicrograph; 1 photograph.

ALFRED O. MILLER, M.D.

Louisville, Ky.

Primary Bone-Forming Tumours and Their Relationship to Skeletal Growth. C. H. G. Price. *J. Bone & Joint Surg.* 40-B: 574-593, August 1958. (University of Bristol, Bristol 1, England)

The author has reviewed several large series of osteochondromas and osteogenic sarcomas in an effort to relate their occurrence to skeletal growth. His cases are selected from the "juvenile period" (below the age of thirty-five) and their features are thoroughly tabulated and discussed.

From their behavior the benign osteochondroma and the osteogenic sarcoma evidently have closely related origins, although the tumor anlagen from which they

derive are quite distinct from each other. A strong male preponderance of the tumors is demonstrable, which is greatest between fifteen and thirty-five years, especially for the long bones. This apparently relates to the fact that there is a greater volume of endochondral bone formation during a longer growth period in boys, and therefore a greater "risk" of tumor in the male.

The predilection of the tumors for the ends of long bones seems simply a matter of formation at the sites where greatest increase in length and size of the bone occurs.

In both sexes the tumors tend to appear at an earlier age in the upper than in the lower extremities. In the other bones they arise at a somewhat earlier age in the female. The author feels that this is due to the relatively advanced skeletal age of girls over boys.

The statistics shown do seem to confirm a relationship to skeletal growth, and to reasonably explain the incidence and anatomic distribution of bone-forming tumors.

Three roentgenograms; 5 photomicrographs; 7 graphs and diagrams; 12 tables.

DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Primary Liposarcoma of Bone. The Angiographic Findings and Doubts as to Its Intramedullary Origin. George Cohen. *Brit. J. Radiol.* 31: 442-444, August 1958. (Johannesburg General Hospital, Johannesburg, Union of South Africa)

The author reports a case of primary liposarcoma of bone in a 47-year-old female. An ill defined hard 6 X 6-inch mass was palpable on the anterior medial aspect of the right thigh. Plain roentgenograms revealed irregular thickening of the cortex of the femoral shaft adjacent to the soft tissue mass, and calcification was present in the latter [not easily seen in the reproductions]. An arteriogram showed no evidence of abnormal vessels, but normal arterioles appeared increased in number and size in the tumor area. The soft-tissue calcifications were noted to be intravascular.

A diagnosis of primary liposarcoma of bone of intramedullary origin was made by three pathologists working independently of one another from both biopsy specimen and the amputated leg. The author, however, believes the lesion to be a periosteal liposarcoma rather than one of intramedullary origin. His opinion is based on the roentgen studies, especially the arteriographic findings. He also observes that the authors of the 9 previously reported cases of primary liposarcoma of bone had similar doubts as to an intramedullary origin.

Three roentgenograms.

SAMUEL B. HAVESEN, M.D.
University of California, S. F.

Circumscribed Serous Spinal Arachnoiditis Simulating Protruded Lumbar Intervertebral Disc. Case Report. George M. Hart. *Ann. Surg.* 148: 266-270, August 1958. (Northwest Clinic, Minot, N. D.)

Circumscribed serous spinal arachnoiditis is a localized, encapsulated collection of fluid in the arachnoid of the spinal canal. It may result from infection, trauma, and pathologic changes in the spine or spinal cord. In many instances no causative factor is found. The lesion produces symptoms and signs of compression of the cord or cauda equina.

Myelography usually demonstrates a ragged, patchy filling defect although smooth defects simulating intra- and extradural tumors have been described. The author reports a case which simulated a protruded intervertebral disk clinically and myelographically.

The lesion is treated surgically and prognosis is good if operation is done sufficiently early that dense fibrous adhesions have not formed.

CAPT. BYRON G. BROGDON, M.C.
Lackland AFB, Texas

Further Observations on the Elastic Mechanism of the Intervertebral Disc. W. G. Horton. *J. Bone & Joint Surg.* 40-B: 552-557, August 1958. (13 Merritt Road, Crofton Park, Brockley, London, S. E. 4, England)

With the polarizing microscope and high-intensity x-ray radiography, it has been possible to show photographically the collagen fibrils and protofibrils which make up the annulus fibrosus and the nucleus pulposus. From a study of thin sections taken from the disks of necropsy subjects of varying ages (from twenty-five to seventy-seven years in this series), certain conclusions emerged regarding make-up and physiology of the disks.

The annulus has been shown to consist of regularly oriented sheets of collagen fibers. When vertical pressures are exerted upon the disks, the stresses are converted to a horizontal thrust by change in the angle of the axis of the fibers in adjacent layers or sheets. This causes an increased girth in the annulus, and also diverts pressure away from the nucleus pulposus.

The fibers tend to proliferate into the nucleus pulposus in older subjects, reducing its gel properties; and with increasing age there may be some reduction in cohesion between the sheets of fibers. This leads to uneven transmission of pressures to the various parts of the annulus and subsequently to physiological dysfunction of the disk.

A simple but revealing explanatory diagram accompanies the article.

Six figures; 2 tables. DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Two Cases of Obstetrical Separation (Epiphysiolysis) of the Upper Femoral Epiphysis. Appearance of Ossification Centre of the Femoral Head in a Fifteen-day-old Child. J. P. Michail, S. Theodorou, K. Houliaras, and N. Siatis. *J. Bone & Joint Surg.* 40-B: 477-482, August 1958. (Orthopedic Clinic, Children's Hospital, Athens, Greece)

Obstetrical fracture of the upper femoral epiphysis is an unusual injury which occurs on rare occasions in association with delivery, especially in breech presentations. As a result of hyperextension, abduction, and rotation during strong traction on the leg, the epiphysis separates, and swelling of the thigh and pain are present thereafter.

Early radiographic diagnosis is difficult, though slight displacement of the upper end of the femur is sometimes identifiable. Later, a calcified hematoma or identification of the separated capital femoral epiphysis after it ossifies permits definite diagnosis.

Two cases are reported, in one of which the ossific nucleus of the femoral head appeared at the exceptionally early age of fifteen days.

Seven roentgenograms.

DON E. MATTHIESSEN, M.D.
Phoenix, Ariz.

Traumatic Effusions of the Ankle and Posterior Subtaloid Joints. W. J. Weston. *Brit. J. Radiol.* 31: 445-447, August 1958. (Hutt Hospital, Hutt, New Zealand)

The anatomy of the synovial pouches of the ankle and posterior subtalar joints and the appearance of traumatic effusions in these joints were investigated by (1) roentgenographic study of 17 ankle joints injected with barium sulfate postmortem and (2) a review of radiographs of 605 cases of ankle injuries.

The normal synovial membranes of the ankle and subtalar joint are not visible on plain roentgen studies. Roentgenograms obtained after injection of opaque material into these joints revealed either a spherical or trapezoid outline of the anterior synovial cavity of the ankle. The trapezoid type is more common and its shape is due to a triangular extension of the synovial pouch on to the lower tibia. There is also an extension of the pouch along the dorsal surface of the talar neck. Since the anterior ligament of the ankle joint is extremely thin, effusions produce their greatest effects anteriorly.

Posteriorly the synovial membrane bulges above and below the invaginating posterior astragalo-fibular ligament, causing the posterior synovial pouch to assume a "figure-3" appearance. Small upward extensions of the synovial pouch occur between the tibia and fibula, sometimes measuring 1.7 cm. above the tibial articular surface. The synovial cavity, as seen on anteroposterior views, extends along each side of the talus and is deeper on the lateral aspect.

The synovial pouch of the posterior subtalar joint is variable in size but in all cases extends further posteriorly than the synovial space of the ankle joint. The cavity starts at the sinus tarsi, runs along the subtalar joint and extends posteriorly along the upper surface of the os calcis. A communication between the ankle and subtalar joints is commonly seen when the ankle synovial cavity is distended during postmortem arthrogramraphy.

Review of 605 cases of ankle injury revealed traumatic effusions of the ankle joints in 220 (40 per cent) of 551 patients. In 54 patients the presence or absence of effusion of the ankle joint could not be determined. Thirty-six (6 per cent) of the 605 patients had effusions into the posterior subtalar joint.

Eight roentgenograms.

SAMUEL B. HAVESEN, M.D.
University of California, S. F.

THE GENITOURINARY SYSTEM

Acute Renal Failure After Intravenous Pyelography in Plasma Cell Myeloma. Pasquale E. Perilli and Harold O. Conn. *J.A.M.A.* 167: 2186-2189, Aug. 30, 1958. (VA Hospital, West Haven, Conn.)

The authors are concerned here with the potential danger of intravenous urography in cases of plasma-cell myeloma and the pathogenesis of acute renal failure so induced. They report the case of a 34-year-old man, subsequently found to have plasma-cell myeloma, in whom intravenous urography was done. Kidney function was apparently normal at the time of the Urokon injection but renal damage became evident within twenty-four hours, with nausea, vomiting, and oliguria. Renal failure was progressive to death, about three months later. The pertinent finding at autopsy was markedly dilated renal tubules, filled, particularly in their proximal portions, with deeply eosinophilic impregnated casts.

In a review of the literature, the authors discovered 4 similar cases with death from acute renal failure in 3, eight to forty days after onset of anuria. In each instance the kidneys at necropsy showed proteinaceous casts plugging the convoluted and collecting tubules. The fourth patient died in uremia after eight months, and in this instance also the tubules were found to be plugged with casts.

It is theorized that in the presence of Bence Jones proteinuria the dehydration produced by fasting and purging incident to urography and the increased concentration of urine caused by abdominal compression, may combine to cause precipitation of the urinary protein within the renal tubules. This internal obstructive uropathy may be prevented by avoiding intravenous pyelography in patients with plasma-cell myeloma or proteinuria of undetermined cause. If acute renal failure is precipitated in these patients by simple dehydration, it is important to assure adequate fluid intake at all times.

One photomicrograph; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Urethrocytography in the Female. T. N. A. Jeffcoate. *J. Fac. Radiologists* 9: 127-134, July 1958. (University of Liverpool, Liverpool, England)

On the basis of personal experience with urethrocytography in over 300 patients, the author believes that in any study only two roentgenograms are necessary: a lateral view of the contrast-filled bladder with the patient sitting at rest and a similar film taken during straining.

The urethra is outlined by an oily opaque medium introduced through an extra-soft rubber catheter. The base of the normal bladder as seen on a lateral view with the patient standing is more or less flat, and situated on a line connecting the lower margin of the symphysis with the fourth sacral vertebra. There is a clearly defined angle between the proximal urethra and the posterior base of the bladder; exact measurement of this angle is not important and in interpretation it is roughly assessed as good, poor, or absent. Normally, when a woman is asked to "bear down," the bladder base descends but the posterior angle is preserved. During voiding, however, the floor of the urethra comes into line with the trigone, and the posterior urethrovesical angle disappears. The bladder also becomes more ovoid in outline, and crenations due to detrusor muscle contraction can be seen on its posterior wall.

In cases of stress incontinence, the most common radiographic finding is absence or poor formation of the posterior urethrovesical angle. The appearance is similar to the normal picture during micturition but other features of voiding, such as ovoid shape of the bladder and crenated outlines, will be absent. Patients with varying degrees of prolapse are continent if the urethrovesical angle is maintained. It has been found that in about 10 per cent of women with stress incontinence the angle is present. Symptoms in these cases may be due to rigidity and inelasticity of the entire urethra, which under normal conditions stays collapsed by virtue of the tone of its involuntary muscle.

In addition to demonstrating the type and site of a lesion, urethrocytography may dictate the necessary surgical cure. For example, it is useless to carry out a sling or Marchetti operation if the posterior angle is present. Errors in interpretation of the study include

failure of the patient to strain down properly; this is avoided if one remembers that with stress the base of the bladder will descend from its position in the resting film. Irritation, which can initiate micturition, should be avoided by using no more than 150 c.c. of a warm solution of opaque material, run in slowly. Sodium iodide (12.5 per cent) in an oily base is least likely to irritate, and foreign bodies such as chains in the urethra should be avoided.

Twenty-four figures, including 15 roentgenograms.

LAWRENCE A. POST, M.D.
University of California, S. F.

Vesicoureteral Reflux in Children. B. W. Jones and James W. Headstream. *J. Urol.* 80: 114-115, August 1958. (University of Arkansas Medical Center, Little Rock, Ark.)

There has been disagreement in the literature on whether or not vesicoureteral reflux occurs in a normal child. In order to evaluate this, the authors subjected 100 children, admitted for nonurologic reasons and without history or findings suggestive of urinary tract disease, to voiding cystography. Of these, only 1 exhibited vesicoureteral reflux. On further examination of this patient a normal excretory pyelogram was obtained, but on cystoscopy 180 c.c. of residual urine and a bladder neck contracture were discovered. A six-month follow-up after surgical correction revealed persistence of the bilateral reflux, but no residual urine.

It is the opinion of the authors that children with normal urinary tracts will not exhibit vesicoureteral reflux on voiding cystograms.

Five roentgenograms.

S. DAVID ROCKOFF, M.D.
University of Pennsylvania

Behavior of the Rectosigmoid Bladder After Radical Cystectomy and Sigmoid Colostomy. N. S. R. Maluf. *J. Urol.* 80: 116-129, August 1958. (Kaiser Foundation Hospital, Los Angeles 27, Calif.)

Isolated rectosigmoid bladders were constructed in 6 patients (4 males and 2 females) following radical cystectomy. Sigmoid colostomies were performed in all 6 patients. The clinical studies described extended over postoperative periods ranging from six months to one year. Proctograms revealed bilateral reflux in the 3 patients who had direct full-thickness end-to-side rectosigmoidostomies, whereas no reflux was observed in the 3 patients who had implants by a combined end-to-side plus tunnel technic. A temporary grade 1 to 2 hydronephrosis was produced by the reflux; however, normal pelvic architecture was demonstrable in these kidneys by intravenous urography.

Capacities of the rectosigmoid bladders ranged from 425 to over 700 ml.; the tidal (or voiding) volumes averaged 125 to 250 ml. Residual urine was negligible. Nocturia (2 to 5 times) and diurnal frequency (every one to two hours) were present, but the daily urinary volumes were not excessive. Except for occasional bed-wetting, incontinence was absent. No appreciable decrease in urinary frequency was obtained by demonstrating to the patients that the capacity of the rectosigmoid bladder far exceeded the tidal volumes, and they continued to void at the first sensation of "pressure" or colic. This discomfort, resulting from gradual filling of the rectosigmoid, was found in all probability to be the result of contractions of the rectosigmoid muscle rather than of rise to intraluminal pres-

sures as such, or gravitation of fluid into the rectum and anal canal, thereby evoking a desire to "defecate." Intravenous Pro-banthine inhibited or prevented the colic.

None of the patients showed any evidence of clinical pyelonephritis although bacteria were cultured from almost all catheterized samples.

Electrolyte disturbances were not severe. A slight hyperchloremic acidosis was present in 4 cases, and the blood urea nitrogen was slightly elevated in 4 cases, the latter observation being explicable on the basis of passive reabsorption of urea through the rectosigmoid. The serum potassium remained at low normal levels after many months, a finding which probably represented a deficiency in total body potassium because the amount of potassium apparently lost in twenty-four hours was minute. The quantity of urea, creatinine, and sodium reabsorbed through the rectosigmoid in twenty-four hours was also estimated. Renal-colonic clearances revealed subnormal creatinine- and urea-clearances; however, normal outputs of urea and creatinine were not evidently affected by the slightly elevated renal loads.

It is concluded that the rectosigmoid bladder can afford an advantageous pouch for the collection and intermittent evacuation of urine, that electrolyte disturbances are minor, and that excision of the superior and inferior hypogastric plexuses in the future may permit larger tidal volumes.

Nineteen roentgenograms; 8 photographs; 4 charts; 4 tables.

H. W. SCOTT, M.D.
University of Pennsylvania

Radiography and Tomography of the Prostate. D. Sichel and E. Blum. *J. de radiol.* 39: 487-493, August-September 1958. (In French) (Hospices civils de Strasbourg, France)

The authors discuss various radiographic procedures such as intravenous urography which are used in studying patients who have possible lesions of the prostate. Studies were carried out with simple radiography and tomography after injecting the bladder with air. Similar studies were made after injecting air into the retroperitoneal space around the prostate. It was finally concluded that about the same amount of information could be obtained by injecting the air into the bladder without injection into the retroperitoneal space.

The authors believe that tomography will furnish some further information concerning the extent and size of prostatic lesions and possible invasion of the bladder wall.

Thirteen roentgenograms; 1 photograph; 11 diagrams. CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

MISCELLANEOUS

The Space Between Stomach and Diaphragm. G. S. Sarin and N. G. Gadekar. *Indian J. Radiol.* 12: 111-114, August 1958. (Irwin Hospital, New Delhi, India)

Normally, the space between lung and the gas in the gastric fundus is less than 5 mm. thick as seen on an x-ray film. This space can be increased by air, fluid, or soft-tissue masses.

Two supradiaphragmatic conditions, left ventricular enlargement and infrapulmonary effusion, may cause an apparent increase in the space. Of subdiaphragmatic conditions enlarging this space, carcinoma of the fundus

of the stomach is most important. Two typical cases are shown. Other abdominal causes are: enlargement of the left lobe of the liver, an extra hepatic lobe, enlargement of the spleen upward and to the right, tumors of the kidney, tumors of the adrenal, and enlargement of the tail of the pancreas.

These conditions should be kept in mind whenever the space between stomach and diaphragm appears increased radiologically.

Nine roentgenograms.

CAPT. HARRIS W. KNUDSON, M.C.
Lackland AFB, Texas

Complications of Adrenocortical Therapy: A Radiological Survey. George Ansell. *J. Fac. Radiologists* 9: 113-126, July 1958. (University of Liverpool, Liverpool, England)

On the basis of a study of 140 patients who received steroids, and a review of the literature, the author considers the major complications of this form of therapy and points out the role of the radiologist in their recognition and management.

In large doses the steroids may produce sodium and water retention with resulting edema, hypertension, and cardiac enlargement. When a patient has pre-existing cardiovascular disease, these changes must be carefully evaluated in regard to their etiology. This same problem occurs in patients with polyarteritis nodosa and systemic lupus erythematosus; one must decide whether pulmonary edema, pleural effusion, or cardiac enlargement represents the natural progression of the disease or overdosage with ACTH or cortisone. If prednisone or prednisolone is used, fluid retention is less likely to occur. The anti-inflammatory reaction of the adrenal steroids leads to the spread of infections, and all patients must be watched closely for unexpected reactivation of pulmonary tuberculosis. Tuberculosis, however, is not an absolute contraindication to steroid therapy provided that the risks are appreciated and simultaneous chemotherapy is given.

One of the more serious complications of adrenocortical therapy is the liability to peptic ulceration and its sequelae. There may be exacerbation of a pre-existing ulcer or development of an acute crater. Clinical evaluation is clouded by the fact that many patients on steroids complain of abdominal pain relieved by alkalies, yet show no roentgen changes. The cause of this pain is uncertain but more vigorous follow-up studies might reveal additional cases of ulceration. From a study of the literature the author feels that there may be a higher incidence of dyspeptic symptoms with the use of ACTH and prednisone than with cortisone and hydrocortisone.

Although colonic perforation has been reported in patients with ulcerative colitis during steroid therapy, the incidence is no greater than in untreated patients. However, steroids mask the clinical picture of perforation and infection, and one must never hesitate to obtain survey films of the abdomen or chest in any patient who, while receiving steroids, has obscure pulmonary or abdominal symptoms. There is still considerable debate about the effect, if any, of cortisone on the roentgen appearance or course of rheumatoid arthritis. Steroid therapy can produce osteoporosis; several instances of spontaneous fractures have been reported, usually in patients already predisposed to osteoporosis and in most cases after many months of therapy. As with other tissues, steroids may predispose to infective

changes in the bones and joints, with masked symptoms. A case of rapidly progressive tuberculous spondylitis in a patient receiving ACTH is illustrated.

A final word of caution is given to the clinician who may want to stop steroid therapy when a complication develops, or before surgery in the mistaken belief that it will interfere with healing. In these periods of stress the patient is in most need of adrenal cortical hormone; if there has been previous steroid therapy, the adrenal cortex becomes hypoplastic and unable to react to stress. These patients will then be liable to develop acute adrenal insufficiency.

Thirty-three roentgenograms; 1 diagram; 1 table.

LAWRENCE A. POST, M.D.
University of California, S. F.

TECHNIC

High Voltage Diagnostic Techniques. Robert D. Shepard, John F. Berry, Jr., and Ollie J. Sparks. *J. Kentucky State M. A.* 56: 663-665, July 1958. (310 S. Limestone St., Lexington, Ky.)

The authors report on their use of high-voltage radiography with its reduced radiation exposure to the patient in various examinations.

In chest studies with high voltages, the shadows of soft tissues are little changed but those of the ribs are greatly diminished, so that other structures are less obscured.

In examinations of the colon, the greater penetration of the high-voltage rays is of "tremendous advantage," being especially effective in detailing the various segments of the bowel, particularly in the obese patient.

In Cholografin studies of the bile ducts, high voltage is a distinct disadvantage, since the concentration of medium is insufficient to allow for good contrast and the duct outline is greatly diminished. Nor did the technic offer any advantages over conventional methods in gall-bladder studies.

In studies of the bones through a plaster cast, the in-

creased penetration of the high-voltage rays seemed to diminish cast detail and to show more clearly the underlying bone. Detection of early healing also seemed to be enhanced.

In order to reduce radiation dosage to both mother and fetus, the authors are now using high-voltage technic in all their pelvimetries. Here one is not concerned with fine bone detail, and the outline of fetal and pelvic bony structures is quite sufficient for accurate measurements.

New Procedures for Examination of the Lymphatic System: Deep Lymphangiography and Lymphofluorescence. P. Leenhardt and R. Colin. *J. de radiol.* 39: 554-556, August-September 1958. (In French) (Centre anticancéreux de Montpellier, France)

The authors tried to perform lymphography of the lower extremity by injecting deep branches of the arterioles of the feet. This method is difficult and gives inconstant results. A method described by Tosatti and Accuncio [reference not quoted] is more satisfactory. This technic consists in exposing a small vein in the external retromalleolar space. A blue dye is injected into the external border of the foot or near the plantar surface of the calcaneus and is taken up by the lymphatics, which then become visible in the retromalleolar space. Following this, injection of an opaque medium allows radiographic visualization.

Lymphofluorescence refers to a second procedure. After identification of the lymphatic vessels, more or less as described above, 2 per cent fluorescein is injected. The extremity is then viewed under a Wood light and the lymphatics seem to display an intensely brilliant fluorescence. This procedure is probably of special interest in studies of functional derangements of the lymphatics such as may occur in patients with thrombo-phlebitis.

Five roentgenograms.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

RADIOTHERAPY

A 45-Million-Volt Linear Accelerator as an Electron Source for the Treatment of Deep-Seated Carcinomas. Erich M. Uhlmann. *Strahlentherapie* 106: 319-333, July 1958. (In German) (Michael Reese Hospital, Chicago, Ill.)

The author briefly traces the history of electron therapy and the development of sources for the utilization of high-speed electrons in the treatment of deep-seated malignant neoplasms. After a discussion of commercially available betatrons, a detailed description of the installation and components of a 45-Mev linear accelerator at the Michael Reese Hospital in Chicago is given. Sufficient details are included for an understanding of the function of the component parts and their interaction. The utilization of a klystron, as developed by Hansen and Ginzton, permitted the installation of an accelerator tube of only 10 ft. in length. Elaborate measures for protection of personnel and patients are described. Unless all protective devices are in operation, the machine cannot be used, and an alarm system indicates any malfunctioning.

After passing the accelerator tube, the beam of electrons is sent through a magnet system, consisting of

a 45° analyzing magnet and a 135° magnet; both rotate in a 90° angle to permit bending of the beam in any direction needed for therapeutic application. By scattering and subsequent narrowing of the beam, a homogeneous distribution of electrons in field sizes up to 18 sq. cm. can be obtained.

The dose distribution is shown in isodose curves produced with energies of 25 Mev, 30 Mev, and 35 Mev. The depth dose curves in ranges between 10 Mev and 35 Mev show the rapid decrease in depth penetration to zero with a good approximation to the postulated formula $(Mev/2) - 0.5$ cm. Consequently, a 20-Mev electron beam will penetrate not more than 9.5 cm. effective depth, and a 30 Mev not more than 14.5 cm. effective depth.

Examples of utilizing electron therapy in the range between 25 Mev and 35 Mev in the treatment of carcinomas of the esophagus, the lung, and the uterus are given. The preliminary therapeutic results were good, and the tolerance to this form of therapy excellent. The skin reactions were minimal, and no systematic reactions were encountered following application of 7,000 to 8,000 r to the tumor, through two fields.

[Detailed descriptions of this linear accelerator have appeared in *RADIOLOGY* 66: 859, 1956, and 67: 263, 1956.—Ed.]

Fourteen figures, including 4 roentgenograms.

HERBERT C. POLLACK, M.D.
Chicago, Ill.

Brainstem Tumors in Children. Patrick F. Bray, Sidney Carter, and Juan M. Taveras. *Neurology* 8: 1-7, January 1958. (P. F. B., University of Utah College of Medicine, Salt Lake City 15, Utah)

Tumors arising within the brain stem are more common in children than in adults. The onset of neurologic symptoms and signs is frequently insidious and increased intracranial pressure usually does not develop until late in the course of the disease, if at all. This slowly developing picture and the wide range of neurologic signs frequently make early diagnosis difficult.

Forty-eight cases with the diagnosis of brain-stem tumor have been seen over the last twenty-four years at the Neurological Institute and Babies Hospital, Columbia-Presbyterian Medical Center, New York. The age at the onset of symptoms ranged from two to sixteen years, with an average of six years and eight months. Forty-seven patients had a disturbance in gait, but it is frequently impossible to differentiate a gait disturbance due to weakness associated with corticospinal tract involvement from ataxia due to a cerebellar pathway lesion. A little over half the patients had a squint, and in slightly less than half there were vomiting, headache, and speech disturbance. Pyramidal tract signs were common. Involvement of multiple cranial nerve nuclei was the rule. The most commonly involved cranial nerve was the seventh (45 patients), and 25 per cent of all patients showed a facial diplegia at some time during their disease. Both the ninth and tenth nerves were affected in 39 patients, accounting for the common symptoms of dysarthria and dysphagia. Sensory fifth involvement was seen in 31 cases, whereas the motor branch of this nerve was implicated in only 13. Sixth nerve palsies was observed in a little over half the cases. Seven patients had either unilateral or bilateral deafness. Horizontal nystagmus was seen in over half the series, and vertical nystagmus in 29 per cent. Seventeen patients had papilledema at some time in the course of the disease. Cerebrospinal fluid pressure measurements were recorded in 10 patients; the average value was 155 mm.

Thirty-four patients had a simple roentgen examination of the skull. Evidence of increased intracranial pressure was found in 7 of these (suture separation in 5 and changes in the sella turcica in 2). The typical findings on pneumoencephalography include posterior and upward displacement of the aqueduct of Sylvius and the fourth ventricle ("bowing" of the aqueduct), as seen in the lateral projection. In this same view the anterior margin of the fourth ventricle is sharply defined and the cisterna pontis may be narrowed. In instances where the tumor is quite large, one may see elevation of the posterior part of the third ventricle. In 30 of the 48 cases air contrast examinations made it possible to estimate the size of the lateral or the third ventricle. Ventricular dilatation was present in 20 of these 30 patients, but was most frequently slight or moderate, even in patients with large tumors.

Thirty-nine of the 48 patients lived long enough to receive at least one course of radiotherapy. In the cases treated prior to 1952, 1,000 to 1,200 r was adminis-

tered over a period of twelve to thirty days, depending upon the patient's condition. This dose was repeated two or three times at six-week intervals. In the past four years an effort was made to deliver a single tumor dose of 4,000 r to adults, in twenty-eight days. In infants under two years of age, half of the adult dose is given; between three and four years of age, 75 per cent, with a gradual increase with age until at eight years the full adult tumor dose is employed.

Twenty-four patients who received one or more courses of roentgen therapy were followed until death. Survival time in these patients was computed from the first hospital admission date, when the diagnosis was established, to the date of death. The average survival was nine months. Fifteen of the 24 patients were thought to have shown clinical improvement following treatment. There was a striking consistency in the time it took for clinical improvement to appear. With the first course of irradiation, practically all patients manifested improvement between three and six weeks after the beginning of treatment. Twelve of the patients who showed clinical improvement in response to the initial irradiation received a second course of therapy; 7 of these were thought again to show some signs of improvement. No children who failed to respond to the first course showed improvement following subsequent series. Eight patients were alive at the time of the report, one month to thirteen years after treatment.

The management of the patient with a brainstem tumor is challenging and generally discouraging. Surgery has little to offer. While the authors' results with radiotherapy have certainly not been dramatic, the repeated experience of having induced a clear-cut remission of neurologic symptoms and signs for a short period deserves emphasis. It should be kept in mind that there is a lag, usually of three to six weeks, between the institution of treatment and the initial signs of improvement. The signs of improvement usually observed were partial clearing of cranial nerve and pyramidal tract abnormalities. With the higher doses recently employed, remissions have been produced in a greater percentage of patients. It is questionable whether there is any increase in survival time. Also, the recurrence of symptoms or signs seems to take place at approximately the same rate.

Nine figures, including 2 roentgenograms.

Radiotherapy for Malignant Tumours of the Thyroid. G. W. Blomfield. *Proc. Roy. Soc. Med.* 51: 522-525, July 1958. (Sheffield National Centre for Radiotherapy, Sheffield, England)

A series of 100 consecutive cases of thyroid cancer seen over a nine-year period and followed for three or more years is analyzed, and extensive data are presented in tabular form. Some points of interest arising from the analysis include a 4:1 ratio of female to male patients; a history of goiter in one-fifth of these series; co-existent hyperthyroidism in 7 cases. By far the most frequent complaints were swelling of the thyroid and mass lesions in the neck, frequently with pressure symptoms. Histologically the tumors were classified as papillary, follicular, and undifferentiated carcinoma, with a small group designated "other." More than two-thirds of the patients with papillary growth survived over five years, while only one-fifth of those with undifferentiated growths lived as long.

About 60 per cent of the patients had metastases at some time during their observed course and the per-

centage of metastases increased with the length of follow-up. By far the most common metastatic sites were the adjacent cervical nodes. Spread to the lungs and bones occurred but less frequently. Surgery combined with deep x-ray therapy yielded 2 per cent five-year survivals while x-ray therapy alone showed survival of only 18 per cent. It is pointed out, however, that those cases treated by irradiation only were almost all undifferentiated and/or advanced growths of unfavorable type. Radiotherapeutic technics are not described. The author feels that extension of the tumor into the thoracic inlet forms a very strong indication for supervoltage irradiation. Only 7 of the 100 cases appeared to satisfy the criteria accepted for I^{131} therapy. All of these had one or more large doses of I^{131} but in only 1 was a very favorable result obtained.

The author concludes that little account can be taken of survival statistics alone in assessing the value of radiotherapy or surgery of carcinoma of the thyroid. This is so because of the wide variation of technics used and the wide biologic differences of these tumors. He believes that more valuable criteria are relief of symptoms and degree of objective improvement.

Six tables.

JAMES W. BARBER, M. D.
Cheyenne, Wyo.

Surgical Considerations in Treatment of Malignant Disease of the Thyroid Gland. Geraldine Barry. Proc. Roy. Soc. Med. 51: 521-522, July 1958. (Royal Free Hospital, London, England)

The author's remarks are based upon her experience with 57 cases of thyroid carcinoma seen personally. Thirty-one of these patients presented a solitary nodule in the thyroid found on pathologic examination to be malignant, usually papillary adenocarcinoma. In several cases surgical removal of the nodule was followed by a course of "masterly inactivity," and only 2 of these subsequently showed local recurrence; there were no distant metastases. In 2 patients total thyroidectomy was done following the pathologic report of malignant tumor, but the author has abandoned this procedure as difficult and probably unnecessary. She believes that removal of the nodule and identification of the tumor should be followed by a vigorous course of deep x-ray therapy, or possibly I^{131} . No recurrences have developed in cases so treated.

In the group of patients demonstrating frankly malignant disease with spread outside the thyroid proper, the author advocates total thyroidectomy and removal of involved adjacent cervical nodes. She does not feel that the usual block dissection is indicated or necessary, nor does she hesitate knowingly to leave behind a small amount of malignant tissue to be subsequently managed by radiotherapy. Of 17 patients with growths involving the trachea, esophagus, skin, or strap muscles, treated by total thyroidectomy and removal of nodes, followed by a vigorous course of deep x-ray therapy, only 1 died from recurrence, but the interval of follow-up is not stated.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Results of Radiation Therapy of Esophageal Carcinoma at the Medical University Clinics in Erlangen (1946-1955). Gunther Barth, Walter Brichzy, and Helmut Jaxtheimer. Strahlentherapie 106: 523-537, August 1958. (In German) (Medizinische Universitätsklinik Erlangen, Germany)

The authors report on 224 inoperable cases of esoph-

ageal carcinoma which received palliative roentgen therapy from 1946 until 1952. There were 180 males and 44 females in the series. Most patients were in the seventh decade, the men being somewhat older than the women. Only 4 per cent were well nourished, 28 per cent were in fair condition, 52.4 per cent in poor condition, and 15.6 per cent were already cachectic. Distant metastatic lesions were found prior to treatment in 9 patients and later in 7 others.

The lower esophagus was involved in the majority of cases. The higher the lesion was located in the esophagus, the more advanced was the emaciation and the shorter the interval between the first symptoms (dysphagia, retrosternal pain, weight loss) and the institution of roentgen therapy. This interval ranged from two weeks to two years, with an average of three to six months. Because of stenosis, gastrostomy was necessary prior to treatment in 14 cases and later on in 22 other cases.

From 1946 until 1948 only stationary portals were used, with cross-fire technic and four to six converging fields. In 1949 rotational therapy with continuous fluoroscopic control was begun. Technical factors were 220 kvp, 20 ma, 0.36 mm. Cu filtration, and 0.86 mm. Cu h.v.l. Single doses began with 120 to 150 r and were gradually increased to 200 r and even to 250 r. The aim was a total tumor dose of 4,000 to 5,000 r, which, however, could not be tolerated in many advanced cases. In a number of cases a total of 8,000 r or more was delivered during a period of six to eight weeks. Rotational therapy was better tolerated than cross-fire irradiation through stationary fields. In only 10.3 per cent of patients treated with stationary fields, could more than 6,000 r be applied, but doses of this magnitude were tolerated by 53.3 per cent of those receiving rotational therapy.

An effect of roentgen therapy could be noticed only after a minimum dose of 4,000 r. Favorable responses were limited to cases in which the growth was not too far advanced and the general condition was still fair at the beginning of treatment. A survival of more than two years ensued only with a total dose of at least 6,000 r. Of the 9 two-year survivors, 8 followed rotational therapy. Second, third, and fourth series of treatments proved to be increasingly less effective.

Since even the most advanced cases had been accepted for therapy, the results were far from impressive: 31.2 per cent of the patients died within the first three months after treatment was begun; 80 per cent did not survive the first year, and 95.8 per cent were dead within two years. Only 4.2 per cent survived more than two years. Patients with the shortest history had the shortest survival. Contrary to expectations, survival of the well nourished was surprisingly short, while the cachectic patients and those with metastatic lesions and gastrostomy lived longer. The lower the lesion was located in the esophagus, the longer was the survival.

Nine tables.

ERNEST KRAFT, M.D.
Northport, N. Y.

Does Supplementary Roentgen Castration have a Noticeable Therapeutic Effect in Breast Cancer? Andreas Siegert. Strahlentherapie 106: 567-579, August 1958. (In German) (Universitäts-Frauenklinik Erlangen, Germany)

Surgical castration in addition to radical mastectomy for breast cancer was proposed some seventy years ago, while the history of roentgen castration dates

back some forty years. Nevertheless, the procedure has not met with uniform acceptance. Opponents claim (1) that beneficial effects have not been proved and (2) that symptoms arising from an artificial menopause form a distinct contraindication.

The author evaluates the material of the Erlangen Clinics from 1918 until 1945. During this period 1,582 cases of mammary carcinoma were seen, but only 607 of these were in premenopausal patients. Of this latter group, 347 were treated with and 260 without roentgen castration. It was found that patients with severe menstrual bleeding and premenstrual swelling of the breasts did very poorly unless mastectomy was supplemented by ovarian irradiation.

On the basis of personal experience and an elaborate statistical analysis the author concludes that castration is justified in all premenopausal patients with breast cancer. The favorable effect has been statistically established, although the exact mechanism and causal relationship are still not clearly understood. All objections to an artificial menopause appear to be of little significance when one considers that periods free from recurrences and/or metastatic spread can be prolonged by this means.

One chart; 1 graph; 5 tables.

ERNEST KRAFT, M.D.
Northport, N. Y.

Current Treatment of Carcinoma of the Cervix. H. L. Kottmeier. *Am. J. Obst. & Gynec.* **76**: 243-251, August 1958. (Radiumhemmet, Stockholm, Sweden)

Five-year results are presented for 1,081 patients with carcinoma of the uterine cervix treated at the Radiumhemmet (Stockholm) with individualized technique in the three years, 1949-1951. The "apparent" recovery rate was 51.1 per cent for Stages I-IV. This compares with 42.5 per cent for the period of 1946-1948, and 42.3 per cent for 1936-1945. For Stage I the five-year apparent recovery rate was 89.0 per cent; for Stage II A, 64.4 per cent; for Stage II B, 45.2 per cent; for Stage III, 33.5 per cent; for Stage IV, 7.8 per cent.

Irradiation was the primary treatment in all cases of invasive carcinoma. Intrauterine and intravaginal radium applications were carried out so that the best possible dosage distribution was applied to the extent of the carcinoma. Careful pelvic examination, urography, and sometimes venography were necessary to demonstrate the extent of the disease. With the radium application in place, dosage rate was determined with an ionization chamber in the bladder and rectum. Using such information and isodose curves for various radium systems the treatment was individualized and additional external beam therapy planned. Persistent or recurrent carcinoma was most often treated by surgery or electrotherapy; for metastatic suburethral or vaginal deposits reirradiation was used.

Four-year cure rates of 64 per cent and 41 per cent in cases with good and poor sensitivity response (SR), respectively, were obtained in 99 cases treated in collaboration with Drs. Ruth and John Graham.

Three roentgenograms; 3 diagrams; 1 table.

ROBERT L. EGAN, M.D.
University of Texas, Houston

Transperitoneal Pelvic Lymphadenectomy Following Supervoltage Irradiation for Squamous-Cell Carcinoma of the Cervix. Felix N. Rutledge and Gilbert H. Flet-

cher. *Am. J. Obst. & Gynec.* **76**: 321-334, August 1958. (M. D. Anderson Hospital and Tumor Institute, Houston, Texas)

One hundred consecutive patients with Stage III squamous-cell carcinoma of the cervix received high doses of radiation to the whole pelvis from the 22-Mev betatron (average dose 6,000 r in six weeks), supplemented by 3,000 to 5,000 mg. hr. of intracavitary radium. Three months later, pelvic lymphadenectomy was carried out.

Lymph nodes containing viable squamous-cell carcinoma were found only within the irradiated field in 5 cases, only outside the irradiated field in 8 cases, and both inside and outside the irradiated field in 9 cases. Ghost cells of squamous carcinoma in lymph nodes were demonstrated in 4 cases.

The authors consider an estimate of 50 per cent for positive nodes in Stage III cervical carcinoma to be conservative. Their incidence of 22 per cent, including common iliac and periaortic nodes, or 14 per cent for pelvic-wall nodes proper, is statistically highly significant.

This series indicates that high-dose whole-pelvic irradiation is effective in destroying metastatic squamous-cell carcinoma of the cervix on the pelvic wall proper.

One roentgenogram; 13 photomicrographs; 2 drawings; 8 tables.

ROBERT L. EGAN, M.D.
University of Texas, Houston

Dietary Regime During Radiation Therapy for Carcinoma of the Uterus. Caroline N. Turner. *M. J. Australia* **2**: 227-228, Aug. 16, 1958. (Peter MacCallum Clinic, Melbourne, Australia)

Fifty patients undergoing radon and roentgen therapy for carcinoma of the uterus were placed on a dietary regime to observe its effect on the diarrhea and tenesmus which so often accompany irradiation. During the period when radon was in position in the vagina, the patients received low-residue diets. In the course of the subsequent external roentgen therapy (approximately four weeks) the diet was made as bland as possible to decrease irritation of the intestine. Fluid intake, protein supplements, and vitamins were maintained at adequate levels.

Details of the diets used are described. Low-residue diets included such foods as eggs, soft meats, milk, butter, refined cereals, and sugars. Bland diets eliminated vegetable and fruit fibers, coarse meats, and spicies.

Of the 50 patients on the specified diets, 30 had minimal or no distressing symptoms of diarrhea or tenesmus. Only 2 had severe symptoms.

A trial of the similar diets for individuals undergoing supervoltage roentgen therapy for carcinoma of the bladder gave equally successful results.

One table. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Palliative Radiation Therapy: Use in the Advanced Cancer Patient. Milton Shoss. *Missouri Med.* **55**: 849-853, August 1958. (937 Broadway, Cape Girardeau, Mo.)

At present palliative therapy is eagerly accepted for all incurable diseases except cancer, although prolongation of a useful and enjoyable life is a noble aim in this disease as in nephritis, hypertension, diabetes, arteriosclerosis, chronic heart disease, etc.

Before any consideration of therapy can be under-

taken, positive proof of the diagnosis of cancer must be made histologically. The pathologist, radiologist, surgeon, and family physician should then enter into a group consultation to determine whether or not any given case is amenable to palliation. The general condition of the patient is of utmost importance and only in cachectic patients in a terminal state is it felt that therapy is wasted.

Evaluation of results should include consideration of the objective local effect, clinical symptoms, general condition, absolute survival time from the institution of irradiation, and extent of terminal distress.

Three case reports illustrating unexpectedly good results of what was originally intended to be palliative radiation are given. (1) A woman twenty-nine years old when first seen had led a normal life for seven years at the time of the report, after therapy of a large retroperitoneal reticulum-cell sarcoma. (2) Definite palliation was effected over a period of seven months before death in a 36-year-old male with a relatively radioresistant mucinous carcinoma of the large bowel. (3) In June 1955, a 67-year-old white female was seen with advanced carcinoma apparently arising from the ovary and extending throughout the peritoneal cavity. After completion of radiotherapy she returned to her previous occupation and, when seen by the author in March 1958, had required no further definitive therapy.

The Treatment of Female Sterility with X-Ray Therapy Directed to the Pituitary and Ovaries. Ira I. Kaplan. *Am. J. Obst. & Gynec.* 76: 447-453, August 1958. (755 Park Ave., New York 21, N.Y.)

In view of thirty-two years of experience in the treatment of infertility and sterility, and the results achieved in the production of healthy children and grandchildren, the author's current appraisal would indicate that this therapeutic procedure is justifiable. Of 636 treated patients, 341 conceived, bearing 540 children following irradiation. There was no overall increase in miscarriage or fetal abnormalities.

[See a later report by the same author in *Radiology* 72: 518, 1959.—Ed.]

Seven tables.

ROBERT L. EGAN, M.D.
University of Texas, Houston

The Repudiation of Low-Dosage Irradiation of the Ovaries. S. Leon Israel. *Am. J. Obst. & Gynec.* 76: 443-446, August 1958. (2116 Spruce Street, Philadelphia 3, Penna.)

The author believes that low-dosage irradiation of the pituitary gland and ovaries for the correction of anomalies of menstrual rhythm and anovulatory sterility, an empiric effective and economical form of therapy, should be re-evaluated. His own conclusion is as follows: "When serious-minded scientists of the atomic age issue universal recommendations aimed at decreasing the hazards of ionizing radiation to future generations of mankind, we cannot help but be persuaded morally to discontinue low-dosage irradiation of the gonads. We must do this even if the hazards are theoretical and are minimized by the fact that such therapy is applied to but few women of the world's population."

One table.

ROBERT L. EGAN, M.D.
University of Texas, Houston

Role of Radiotherapy in Calcaneal Spur. O. N. Saxena. *Indian J. Radiol.* 12: 115-116, August 1958. (S. N. Hospital, Agra, India)

The author reports his results in 9 cases of painful calcaneal spur receiving x-ray therapy. Two fields, medial and lateral each 7 X 7 cm., were used over the heel, each being given 600 r in a day, for a midline dose of 750 r. The physical factors were: 200 kv, 15 ma, 0.75 mm. Cu plus 1.0 mm. Al filtration; 50 cm. distance.

In 8 cases pain was relieved within eight days, and there had been no recurrence of symptoms in a two year period. One case did not respond.

CAPT. BRYON G. BROGDON, M.C.
Lackland AFB, Texas

RADIOISOTOPES

The Thyroidal Accumulation of Radioiodine as a Clinical Test for Hyperthyroidism. I. J. L. Goldberg and Elizabeth A. Fitzsimons. *Brit. J. Radiol.* 31: 428-432, August 1958. (West London Hospital, London, W. 6, England)

Using a collimated Burndep 1192A scintillation counter at 24.7 cm. from the skin, the authors set about to compare the various tests for radioiodine accumulation in the thyroid. For the study 130 persons (30 hyperthyroid and 100 euthyroid) were used. The diagnosis was decided on clinical grounds and the test results, including basal metabolic rate, protein-bound radioiodine at forty-eight hours after a tracer dose, and the protein-bound I^{131} in most cases. The response to treatment over a period of observation of at least six months and, in some cases, more complex thyroid function tests were also taken into account.

On a comparative basis the least satisfactory test was the 24-hour radioiodine uptake. The other seven thyroid function tests investigated correlated well when thyroid clearance was the reference test, and all adequately distinguished between euthyroid and hyperthyroid states.

The inaccuracy of the twenty-four hour uptake test

is attributed to the fact that some radio-thyroxine is formed soon after administration of the tracer dose and is discharged into the circulation, thus lowering the level in the gland at the twenty-four-hour calculation. There is a close correlation between the "T" index and the 8- to 24-hour excretion fraction. Both these tests are based on kidney clearance of radioiodine and require the intelligent co-operation of the patient. The thyroid clearance test is still probably the most accurate one available but is intricate and causes the patient considerable inconvenience. The thigh/neck clearance and Berson clearance are also complex tests and do not increase accuracy of results. The two-hour uptake test necessitates close attention to counting technic.

The neck/thigh ratio and the two-hour uptake have certain advantages over the relatively simple eight- to twenty-four-hour excretion fraction and the "T" index. The results are available the same day and the tests may be performed with I^{132} , which has a half-life of only 2.33 hours, resulting in much less patient radiation than when an equal number of microcuries of I^{131} must be used.

Two graphs; 2 tables. SAUL SCHEFF, M.D.
Boston, Mass.

A Comparison of Radioiodine Tests in the Diagnosis of Hyperthyroidism. A. W. G. Goolden. *Brit. J. Radiol.* **31**: 433-436, August 1958. (Hammersmith Hospital, London, W. 12, England)

The object of this paper was to compare three basic radioiodine tests in 70 patients three to four months after treatment with I^{131} for thyrotoxicosis. Observations on 50 untreated patients are also included. The tests were: thyroid clearance; the T index, based on urinary excretion of the isotope; determination of the protein-bound I^{131} in the plasma at forty-eight hours.

The most satisfactory test in the hands of the author was the thyroid clearance test, for which the rate of change of thyroidal I^{131} is divided by the plasma concentration of I^{131} . This test is perhaps no more accurate than the fractional urinary excretion or "T" test in untreated patients, but is rapid and convenient despite the necessity for intravenous injection of the isotope and withdrawal of blood on a second occasion. It is much more sensitive than the other two tests in separating residual hyperthyroidism from the euthyroid state in patients treated with I^{131} . The urinary fractionation test, because of the time required and need for patient co-operation, is subject to various errors. The forty-eight hour test for plasma PBI^{131} , though it may serve to separate hyperthyroidism from the euthyroid state, gives readings in treated patients too high to be useful.

SAUL SCHEFF, M.D.
Boston, Mass.

Factors Affecting the Choice of a Routine Radioactive Iodine Test for Thyroid Activity. N. Howard, Joan M. McAlister, and M. B. McEvedy. *Brit. J. Radiol.* **31**: 437-438, August 1958. (University College Hospital, London, W. C. 1, England)

The more common tests involving thyroid function which require measurements at times not exceeding four hours after administration of radioiodine are the two-hour uptake, four-hour uptake, thyroid uptake rate, thyroid clearance rate, and neck-to-thigh ratio. A delayed test measures the thyroid uptake of the isotope at twenty-four hours. Tests of urinary excretion and the measurements of total plasma activity or protein-bound activity at twenty-four to forty-eight hours all require longer periods of time and repeated visits to the hospital in addition to necessitating a greater degree of patient co-operation.

The authors studied 139 patients who were divided on final clinical assessment into euthyroid and hyperthyroid groups. No case with less than a one-year follow-up was included. They found an almost 10 per cent overlap of euthyroid and hyperthyroid patients by using the two-hour neck-to-thigh ratio test while measuring the two-hour percentage uptake as well. This overlap is about the same as with other methods. The two tests can be completed within less than an hour and thus permit the use of I^{132} , which has a short half-life and results in total patient radiation one-thirtieth that caused by an equal dose of I^{131} .

Two figures. SAUL SCHEFF, M.D.
Boston, Mass.

Basal Metabolic Rate, Protein-Bound Iodine and Radioactive Iodine Uptake: A Comparative Study. Hugh F. Ludecke. *Ann. Int. Med.* **49**: 305-309, August 1958. (Morristown Memorial Hospital, Morristown, N. J.)

The diagnosis of typical thyroid dysfunctional states

is usually not difficult from either a clinical or a laboratory standpoint. There are, however, some patients in whom hypothyroidism or hyperthyroidism is suspected, but the clinical picture is not complete or clear, and the laboratory tests are in disagreement.

A comparative study was made in 77 suitable patients of the basal metabolic rate (BMR), protein-bound iodine (PBI), and radioactive iodine up-take (RAI). The BMR was determined with a standard, commercially available machine (Sanborn). The normal values ranged between -10 per cent and +15 per cent. The PBI was determined by the method of Zak as modified by O'Neal and Simms (Am. J. Clin. Path. **23**: 493, 1953). Normal values were between 4.5 and 7 micrograms. The RAI was estimated after an oral dose of 15 microcuries by counting over four different areas after a twenty-four hour period. The lower limit of uptake was considered to be 20 per cent.

The final results indicated a 10 per cent error rate for the BMR, 6 per cent for the RAI, and 2.5 per cent for the PBI. It was concluded that, for a routine test, PBI is to be preferred because it is less subject to error, easier for the patient, and, in the author's hospital, less expensive. However, it is agreed that, when difficult problems in thyroid disease are encountered, all available tests of thyroid function may be necessary for proper evaluation of the patient.

Two tables. HARRY HAUSER, M.D.
Cleveland Metropolitan General Hospital

Radioiodine in the Treatment of Thyroid Carcinoma. A. W. G. Goolden. *Proc. Roy. Soc. Med.* **51**: 525-528, July 1958. (Hammersmith Hospital, London, England)

Of 102 patients with thyroid cancer referred to Hammersmith Hospital for radiotherapy during a six-year period, only 14 had metastases clearly shown to concentrate radioiodine, but 25 patients were given at least one therapeutic dose of the isotope. Radioiodine should not compete with surgery as the primary method of treatment and all operable cases should be treated by excision whenever feasible.

Patients with follicular carcinoma are the best candidates for radioiodine therapy. In about half of these cases metastases are present when the patient is first seen. Ordinarily thyroid ablation must be carried out, either by surgery or by radioiodine destruction, before effective treatment of the metastatic lesions can be expected. It is usually desirable to demonstrate the uptake of iodine by metastatic lesions before a therapeutic I^{131} dose is given. This may be done by counting techniques or by autoradiography of tissue removed after a tracer dose of the isotope. The latter is the most sensitive and discriminating method but is frequently not feasible.

The problem of predicting whether metastases will take up iodine is not an easy one. It can be said as a general rule that anaplastic tumors will not take up iodine or respond to radioiodine therapy, and when skeletal deposits from this type of tumor give rise to symptoms they are best treated by external irradiation.

The function of thyroid carcinoma metastases may be increased by the administration of thyroid stimulating hormone (TSH), but this substance is not always reliable. Patients with physiologically active tumors will frequently show an increased concentration of iodine uptake following a course of antithyroid therapy (propylthiouracil, Tapazole, etc.). When one chooses to administer antithyroid drugs, however, he must be

willing to risk increased tumor activity and growth, a feature which may in some cases be strongly contraindicated.

Of 21 patients with metastasis given radioiodine in this series, 9 showed uptake of iodine in tumor tissue before thyroidectomy and in another 5 patients concentration of iodine in metastases occurred following ablation of the gland. Dosage of I^{131} is admittedly empirical. The author uses 150 to 200 mc as the usual initial dose followed in three to four months by a similar dose as long as any uptake by the tumor tissue occurs. The total cumulative dose is not carried beyond 600 mc. Patients treated with radioiodine should always be maintained on a full replacement dose of thyroid hormone both in the intervals between treatment and after treatment is completed.

In addition to the well recognized complication of bone marrow depression following radioiodine therapy, the author mentions the occurrence of radiation pneumonitis and fibrosis.

It is noted that reliable conclusions cannot be drawn as to this type of treatment because of the small series involved and the widely variable natural history of this disease.

One graph; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

I^{131} -Induced Hypothyroidism in Intractable Angina Pectoris. Edwin C. Albright, Parry D. Soder, and Charles W. Crumpton. *Ann. Int. Med.* 49: 271-277, August 1958. (University of Wisconsin Medical School, Madison, Wisc.)

Twenty-four euthyroid patients were treated with radioactive iodine for severe angina pectoris. In properly selected patients with well stabilized disease and no response to conservative treatment, radioactive iodine induction of hypothyroidism afforded excellent results in 62 per cent, and worthwhile results in 33 per cent. Dosage of I^{131} required varied widely. Although the degree of symptomatic improvement of pain usually paralleled the degree of hypothyroidism, exceptions were observed in which considerable benefit occurred without disturbing symptoms of myxedema. No important side-effects were encountered.

In several cases, partial relief of distressing symptoms of myxedema was possible without a significant increase in angina. Occasionally, coronary reserve will not permit any elevation of metabolism. Recurrence of angina after several months or years of hypothyroidism may be anticipated as the coronary disease follows its natural course. Radioiodine-induced hypothyroidism affords very effective and safe palliative therapy in selected patients with angina pectoris.

Two tables.

HARRY HAUSER, M.D.
Cleveland Metropolitan General Hospital

Myelosintigraphy: A Useful Procedure for Localization of Spinal Block Lesions. Charles R. Perryman, Paul R. Noble, and Floyd H. Bragdon. *Am. J. Roentgenol.* 80: 104-111, July 1958. (Mercy Hospital, Pittsburgh 19, Penna.)

Myelosintigraphy with radioactive iodinated human serum albumin (RIHSA) was used by the authors in the examination of 28 patients with spinal lesions. In some of the earlier cases in the series no clinical evidence of a block was present but these are included along with the others for the sake of completeness.

Approximately 300 μ c of RIHSA in 5 c.c. of normal

saline are injected at the time of diagnostic lumbar puncture if that procedure has indicated partial or complete block. If possible, the patient is placed in the knee-chest position, or the foot of the bed is elevated, for at least fifteen minutes. One hour after injection a scan is made, which requires an average of twenty-five minutes. The scintigram thus obtained is oriented as to level by a lead marker on the patient's back. A roentgenogram is obtained with the marker in position and the scintigram is superimposed upon this for localization of the block.

Injected RIHSA does not have to be removed, since it is rapidly eliminated 40 to 50 per cent leaving the cerebrospinal fluid within twenty-four hours. Most of the I^{131} remains protein-bound. Thyroid uptake, which is about 5 per cent, may be prevented by Lugol's solution preferably given twenty-four hours earlier, though a shorter time interval will probably suffice.

In evaluating the scintigram, it is important to recognize that a normal fade-out may occur at the level of the caudal sac. If a low block is suspected, the patient should be elevated to a sitting position for a few minutes prior to scanning.

Of the 28 cases reported, 12 were positive for complete or partial block or interference with circulation of spinal fluid. In 10 of these the findings were verified at operation. One lesion was localized in the fourth lumbar space but was found actually to be in the fifth. The other was diagnosed as arachnoiditis and operation was not done. In 2 of 9 cases reported as negative, small intervertebral disk herniations were found, and in 1 arachnoiditis. The other 6 patients were not operated upon. In 7 cases the results of myelosintigraphy were reported as uncertain. A lesion was found in 3 of these and in the remainder surgery was not performed.

The authors feel the greatest value of myelosintigraphy is in cases with evidence of partial or complete block at the time of spinal tap. Localization was 100 per cent correct in the 9 cases of this type in the series. Lesions too small to interfere with circulation of cerebrospinal fluid are not consistently localized. It is suggested that arachnoiditis may be suspected when there is irregular distribution of activity or a gradual diminution over a segment with a more normal pattern above and below.

Nine roentgenograms, including 8 myelosintigrams; 3 photographs; 1 table. VAHE MEGHROUNI, M.D.
Los Angeles, Calif.

Synthesis and Metabolism of Radioactive Heparin. Harold B. Eiber and Isidore Danishefsky. *Arch. Int. Med.* 102: 189-193, August 1958. (Flower & Fifth Avenue Hospitals, 1 E. 105th St., New York 29, N. Y.)

Heparin is a sulfated mucopolysaccharide normally present in animal tissues and blood. Its activity as an anticoagulant makes it a compound of basic interest in medicine and, consequently, an understanding of its biochemistry and physiology is important. By means of the radioactive tracers, C^{14} and S^{35} , the authors have shown that heparin is synthesized from glucose and inorganic sulfate. Studies with S^{35} demonstrated that heparin has a half-life of three and one-half days. In other words, it takes this amount of time for half of the body heparin to turn over and be renewed.

One fact definitely established by the authors' studies is that heparin is a normal constituent of the blood in concentrations of 0.5 mg. per 100 ml.

It appears that the optimum dosage of heparin for an

adult of 150 lb. weight is 50 mg. every four hours when given intravenously. Larger doses would not proportionately increase the heparin effect and are unwarranted. With intramuscular administration a slightly higher dosage is necessary.

Four figures.

Uncoated Buffered Ferrous Sulfate. Absorption in Man of Radioactive Iron (Fe^{59}) as Ferrous Sulfate Measured Electronically. Alison H. Price, Lowell Erf, and James Bierly. *J.A.M.A.* 167: 1612-1615, July 26, 1958. (1618 Locust St., Philadelphia 3, Penna.)

Ten patients with a variety of diseases received uncoated buffered ferrous sulfate (Fermalox) tablets, orally, tagged with 0.1 mc of $Fe^{59}SO_4$. Each tablet consisted of 200 mg. of ferrous sulfate and 200 mg. of magnesium aluminum hydroxide. Following this, the uptake of iron was measured by counts of radioactivity.

It was found that the uptake of iron was satisfactory in 9 out of 10 cases. The tenth patient was suffering from terminal cancer and presumably the body metabolism was faulty. The radioactive disintegration count rose from an average of 255 per minute per 5 c.c. sample (background count) to as high as 582 per minute (in twenty-four hours).

It is concluded from this study, supplemented by clinical observations, that buffered ferrous sulfate in uncoated tablets (Fermalox) is absorbed quickly from the stomach even in the absence of significant amounts of free acid, and that it is the most satisfactory medication for use in iron deficiency states.

Two tables.

PAUL MASSIK, M.D.
Quincy, Mass.

Radon Retention in Radium-Injected Beagles. C. W. Mays, M. A. Van Dilla, R. L. Floyd, and J. S. Arnold. *Radiation Res.* 8: 480-489, June 1958.

(Radiobiology Laboratory, University of Utah, Salt Lake City, Utah)

Radon (Em^{222}), a chemically inert gas with a 3.8-day half-life, is the first daughter of radium (Ra^{226}). Much of the radon formed from bone-deposited radium is exhaled in the breath, and the importance of measuring this escaping fraction was early recognized. It is essential in evaluating radium toxicity to know not only the radium burden but also the radon retention, which the authors define as "the fraction of radon produced inside the body which disintegrates therein."

Fractional radon was measured by comparing the γ -ray activity of radon daughters (Pb^{214} and Bi^{214}) at the time of death to equilibrium activity obtained with the radon leak sealed off. Radium 186-kev γ -rays were suppressed by counting only those above about 250 kev.

Data on whole-body fractional radon retention in 16 beagles are presented in tabular form.

Fractional radon retention is similar in rats, dogs, and man at equal times after radium injection. It increases with time after radium deposition. This the authors attribute to increase in mineral density, increase in crystal size, and decrease in diffusion coefficient as bone crystals mature.

There was a striking similarity in fractional radon retention from bone to bone in a particular animal. Average fractional radon retention, based on a study of 8 dogs, ranged from 17.1 per cent in the coccyx to 22.0 per cent in the mandible; for the whole body it was 19.6 per cent. The similarity of individual bone retention to skeletal retention did not apply to the teeth, where much lower retention was found.

A mathematical theory expressing fractional radon retention in terms of mineral density, crystal size, and diffusion coefficient is discussed.

Three figures; 5 tables.

RADIATION EFFECTS

Expectation of Life and Mortality from Cancer Among British Radiologists. W. M. Court Brown and R. Doll. *Brit. M. J.* 2: 181-187, July 26, 1958. (W. M. C. B., Western General Hospital, Edinburgh, Scotland)

The implications of the 1956 report by the United States National Academy of Sciences on *The Biological Effects of Atomic Radiation* concerning apparent shortening of the life span of American radiologists compared with other American physicians led to the present study of life expectancy and cancer mortality in the British radiologist population. The causes of death were determined for 1,377 male British radiologists during the sixty-year period from 1897 to 1957.

Since the first formal committee organized by the British groups interested in radiation protection issued its recommendations in 1921, the radiologist population studied was arbitrarily divided into two groups according as the individuals concerned entered the field before or after that year. It was assumed that occupational exposure of the pre-1921 members was excessively high and that the average exposure of the post-1920 members has been within recommended limits.

Figures for the expected death rate in the male British population of comparable social status compared with the death rate in the radiologist population indicated no detectable shortening of life expectancy in

the latter group. As a matter of fact, it was found that the actual number of deaths was less than expected in the radiologist groups although in the pre-1921 group there was some excess of deaths due to cancer. This, however, is not interpreted to mean an increased life expectancy in radiologists due to occupation.

The excess of cancer deaths in those entering the practice of radiology before 1921 was confined to neoplasms of the skin and pancreas and leukemia. Excessive exposure of the skin of pioneer radiologists is well known and subsequent development of skin tumors is well substantiated. The association of leukemia and exposure to ionizing radiations has been explored (see Dublin and Spiegelman: *J.A.M.A.* 137: 1519, 1948. Abst. in *Radiology* 53: 310, 1949). Increased incidence of pancreatic tumors is not readily explained and may be presumed to be an operation of chance in the present study. There was no excess mortality from cancer in those entering radiology after 1920.

Warren: *J.A.M.A.* 162: 464, 1956. Abst. in *Radiology* 69: 159, 1957, studying the average age at death of American radiologists in comparison with physicians not practicing radiology, concluded that there was a five-year reduction in life span attributable to exposure to ionizing radiations. These two groups, however, cannot be compared, since there is a difference in age distribution which is sufficient to account for the re-

ported difference in average age at death. Radiologists on the average enter practice at a later age than other physicians and, since radiology is a relatively young specialty, there are fewer members in the older age groups.

Six tables.

JOHN F. RIESSE, M.D.
Springfield, Ohio

Carcinoma of the Thyroid Following Irradiation of the Neck. David Rabinowitz and J. Katz. South African M. J. 32: 723-725, July 19, 1958. (University of Witwatersrand, Johannesburg, Union of South Africa)

The authors report a case of papillary carcinoma of the thyroid in a 12-year-old African girl developing seven years after she had received irradiation for a lymphosarcoma of the neck. The dosage had been 4,000 r, well above the so-called "minimum carcinogenic dose" of 200 r.

The literature of the association of irradiation to the neck in children and the subsequent development of cancer of the thyroid is reviewed. Mention is also made of the dangers of radioiodine as a diagnostic tool in infancy and childhood in contrast to its apparent safety in adults.

One photomicrograph; 1 photograph.

Radiation Hazards to the Foetus. Lance Townsend. M. J. Australia 2: 289-290, Aug. 30, 1958. (Department of Obstetrics and Gynaecology, University of Melbourne, Australia)

Certain effects of therapeutic irradiation of the mother's pelvis on the fetus *in utero* have been recognized for many years, and further confirmed by the Atomic Bomb Casualty Commission of the U. S. National Research Council. These include abortion, premature labor, and congenital anomalies, particularly microcephaly.

The author's study is mainly concerned with the relationship between irradiation of the fetus *in utero* and later development of leukemia. In 1956 Stewart *et al.* put forward a preliminary report, showing that 15 per cent of 269 cases of leukemia followed x-ray examination *in utero* (Lancet 2: 447, 1956. Abst. in Radiology 69: 159, 1957). The present author reviewed the records of 204 children under ten years of age who had died of leukemia. Questionnaires were sent to these children's parents, and 171 replied. It was found that 7 per cent of the mothers had x-ray examination during pregnancy. The lack of control series, however, makes it difficult to say whether x-ray examination of the fetus *in utero* is contributory to pathogenesis of leukemia. The author's conclusion is that there is no definite evidence that leukemia is produced by x-rays, but that caution is to be used in applying x-rays to pregnant women. On the other hand, if x-ray examination is necessary for maternal or fetal well-being, it should not be withheld.

One table.

J. S. ARAJ, M.D.
Toledo, Ohio

The Contribution to the Gene Material of the Population from the Medical Use of Ionizing Radiations. J. H. Martin. M. J. Australia 2: 79-84, July 19, 1958. (Physics Department, Peter MacCallum Clinic, Melbourne, Australia)

Information from a number of diagnostic x-ray departments on the quantities of films of various sizes used, together with the figures for the annual consump-

tion of x-ray film in Australia, led the author to conclude that 4,800,000 roentgen examinations are carried out in that country annually. The average gonadal dose per examination is estimated to be 123 mr for males and 227 mr for females. For children, who account for some 12 per cent of roentgen examinations in Australia, the average was found to be about 300 mr. On the basis of an average of 15 examinations before the age of thirty, and with allowance for annual mass miniature surveys covering 25 per cent of the population over the age of fourteen, the contribution to the gonads is estimated at just under 150 per cent of natural background.

In another method of calculation, the dose received by a person at a given age is multiplied by the probable number of children to be subsequently conceived by that individual. This technic, which takes into account the age distribution of those persons presenting for x-ray examination, indicates a contribution of 1,525,000 r equivalent genetic dose per annum, some 160 per cent of the background dose.

Manipulation of the technical factors involved or direct protection may reduce the gonad dose to about 30 per cent of the natural background, probably the best that can be presently achieved. Any further lowering of the dose contribution to the gene material of the population must be obtained by a reduction in the number of examinations made or of the films used per study. However, roentgen exposures in Australia increased by about 50 per cent in a recent five-year period, while the population increase for the same period was only 17 per cent. Since diagnostic examinations are estimated to account for 49.5 per cent of the gonadal radiation from all sources and therapeutic radiations for 8.6 per cent, every effort should be made to reduce this medical contribution to radiation. While much can be accomplished by technical changes, a greater improvement must be expected from the exercise of stricter criteria for the employment of x-rays for diagnostic purposes and for treatment of nonmalignant conditions.

Ten tables.

Radiation-Induced Gene Mutation in Adult Female and Foetal Male Mice. T. C. Carter. Brit. J. Radiol. 31: 407-411, August 1958. (Radiobiological Research Unit, Harwell, Berkshire, England)

Current recommendations for protection against the harmful genetic effects of gonadal exposure to man-made radiation, 90 per cent of it due to medical radiology, are based on the assumption that all human germ cells are equally mutable (mutability measured by the number of mutations detected in the progeny). The radiation dose to the gonads of future parents in the British population is more or less equally distributed to post-natal males, post-natal females, and fetuses *in utero* (Osborn and Smith: Lancet 1: 949, 1956. Abst. in Radiology 68: 793, 1957). Also, *Hazards to Man of Nuclear and Allied Radiations*, Her Majesty's Stationery Office, London, 1956). The germ cells in this population which are most likely to be affected by exposure to radiation are spermatogonia in male fetuses and male adults, oögonia in female fetuses, and oocytes in female adults.

Few data are available concerning the mutabilities of these cells in man, but experiments with *Drosophila* and *Zeal* indicate a considerably higher spontaneous and radiation-induced gene mutation rate in the male line of these organisms. Radiation-induced mutation has

been studied in the adult male mouse *Mus musculus* at seven loci following exposure to a high acute x-ray dose (Russell, W. L.: Cold Spring Harbor Symposia on Quantitative Biology 16: 327, 1951). The present author conducted experiments with adult females and fetal males of this species and the mutation rates observed were compared with that found by Russell. Utilizing a cobalt-60 source, a radiation dose of 600 rads fractionated over twelve sixteen-hour periods applied to the adult females resulted in one mutation at the *d*-locus. Fetal males were irradiated with a Siemens therapy unit operated at 250 kvp with a h.v.l. of 1.2 mm. Cu and a dose rate of 70 rads per minute. An exposure dose of 300 rads (the highest dose compatible with a reasonable level of fetal survival) resulted in one mutant at the *p*-locus. Thus only two mutants occurred in these experiments instead of the 17 expected if the mutation rate had been the same as in Russell's experiment. This difference between observation and expectation was assumed not to be due to chance, even though the number of mutants do not follow Poissonian distribution.

Although the author's experiments and that of Russell differed in several respects, only (1) germ cell type and (2) dose rate effect were considered to be important factors in the marked difference in observed mutation rates. Either one or both factors may have been responsible for the discrepancy in the experiment with adult females. Only (1) appeared to be of importance in the experiment with fetal males.

The author makes no attempt to apply this experimental data to man but suggests that the suspicion arises that high mutability following acute irradiation of the adult mammalian male may be a general law. There are two unescapable conclusions: (1) large scale experiments of this nature with mammalian species should be undertaken; (2) shielding of the gonads of male patients from unnecessary radiation "should be a sine qua non in medical radiology."

Four tables.

S. B. HAVESEN, M.D.
University of California, S. F.

Effect of Fractionated X-Ray Irradiation on Spinal Cord of Animals. Alfred Breit. Strahlentherapie 106: 446-450, July 1958. (In German) (Strahlenabteilung des Städtischen Krankenhauses Passau, Germany)

A great number of reports on radiation effects on the brain are available, but very little has been published about effects on the spinal cord. Among these observations was a case of myelomalacia of the cord reported by Stevenson and Eckhard following the administration of 6,000 r to the neck area (Arch. Path. 39: 109, 1945. Abst. in Radiology 46: 105, 1946).

Stimulated by similar clinical experiences, the author investigated histologic changes following spinal cord irradiation in dogs and rabbits. These investigations have shown only that therapeutic doses of x-rays administered by the fractionated technic may entail distinct modifications in the spinal cord. To date the experiments do not permit any definite information concerning radiation tolerance or radiosensitivity. The author hopes to approach this problem in a series of fractionated tests with the help of the electron microscope or by means of clinical-radiological-histological observations over a long period.

Four photomicrographs; 1 diagram.

HERBERT POLLACK, M.D.
Chicago, Ill.

Gastric Lesions in Experimental Animals Following Single Exposures to Ionizing Radiations. G. Brecher, E. P. Cronkite, R. A. Conard, and W. W. Smith. Am. J. Path. 34: 105-119, January-February 1958. (National Cancer Institute, Bethesda, Md.)

Past studies indicate that the stomach is less sensitive to ionizing radiations than the small intestine. In the intestine, functional changes have been noted within minutes, and inhibition of mitosis is evident within hours of exposure to low dosages of whole-body irradiation. Lethal dosages produce partial denudation of the intestinal mucosa, but regeneration is usually complete within a week. At supralethal doses, complete loss of epithelium leads to extensive fluid loss and, in most species, to death in three to four days. No similar early lesions have been observed in the stomach following single exposure of the whole body to radiation, though changes in gastric motility have been demonstrated.

Recently, plasma transfusion, marrow transplants, and the administration of antibiotic agents have prolonged the survival of dogs, rats, and hamsters, following exposures that killed unprotected animals in three to six days. In these animals gastric lesions developed two to three weeks after irradiation. Following the single exposures, the time sequence of the development and healing of gastric lesions was studied and compared with the lesions of the small intestine in the same animals.

In one experiment dogs were given whole-body irradiation by a Co⁶⁰ source with 1,200 to 1,700 r. In another, the stomach was irradiated with roentgen rays. Rats, too, were given roentgen irradiation (800 or 900 r); within an hour of exposure, they were joined in parabiosis with nonirradiated litter mates. Hamsters were exposed to 1,160 r. Some animals had one leg shielded during irradiation; others received an intracardiac injection of spleen and bone marrow within a few hours of exposure.

Epithelial changes in the gastric mucosa developed about two weeks following single supralethal exposures to irradiation. These changes were quite similar to those occurring earlier in the small intestine. Regeneration proceeded from the neck of the glands and was comparable to the regeneration of small intestine mucosa from surviving crypt epithelium. Occasionally, the direct damage was severe enough to lead to ulceration, even after local irradiation and in the absence of agranulocytosis and hemorrhage. This was in contrast to the late ulcers appearing in the regenerated mucosa of the small intestine, which were associated with hemorrhage or represented direct sequelae of the pancytopenia that follows lethal irradiation.

Twelve photomicrographs.

Radiation-Induced "Dental Death" in Mice. A. C. Upton, R. F. Buffet, J. Furth, and D. G. Doherty. Radiation Res. 8: 475-479, June 1958. (Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.)

The relatively high radiosensitivity of tooth-forming cells, first demonstrated more than fifty years ago, is now well known. Although large amounts of radiation may adversely affect mature teeth, developing teeth are injured by relatively small doses. An investigation has been made of the effects of irradiation on the teeth of mice, in which the incisors continue to grow throughout life to compensate for mechanical wear.

Nine- to ten-week old RF and LAF₁ mice were given a single dose, to the head, of 500 to 1,800 r of 250-kvp x-rays of 100 to 137 r/min. Other radiation factors were: for RF mice—30 ma, TSD 93.7 cm., 3 mm. Al added filtration, and h.v.l. 0.44 mm. Cu; for LAF₁ mice—15 ma, TSD 50 cm., and no added filtration.

Defects in the incisor teeth of the mice were found after exposure of the head to 1,250 to 1,800 r. The time of onset of the dental defects varied with the dose of radiation, all animals exposed to 1,350 r exhibiting changes within seventy days after exposure. Mice affected severely were unable to feed adequately on food pellets and starved to death unless provided with a soft diet.

Intraperitoneal injection (before irradiation) of 2-mercaptoethylguanidine, HBr, which lowers the susceptibility of mice to x-ray-induced death, lessened the extent of radiation injury to tooth-forming cells.

Four figures.

Lipid Metabolism in X-Irradiated Mice and Rats. Roy B. Mefford, Jr., William W. Webster, and Melvin A. Nyman. *Radiation Res.* 8: 461-465, June 1958. (Biochemical Institute, University of Texas, Austin, Texas)

Previous work has indicated that progressive changes occur in the lipid metabolism of animals after irradiation. The present report is concerned with the concurrent time course of changes in cholesterol and fatty acid metabolism in intact rats and mice after x-irradiation. Male Sherman strain rats and DBA/2 Jax mice were used in the investigation. Rats received 500 r and mice 425 r. Both groups of animals showed significant changes in the specific activities of total nonsaponifiable lipids, cholesterol (digitonide-precipitated), and fatty acids. Fatty acids were elevated by the sixth day but by the ninth and fifteenth days (mice and rats, respectively) these had returned to control levels. The specific activities of the cholesterol were less variable, but they were significantly low on the ninth day in the mice and the fifteenth day in the rats. Cholesterol and fatty acid metabolism were quite different; the metabolism of the solid and liquid fatty acids were quantitatively different.

Two tables.

Histological Response of the Duodenum to X-Irradiation in Hypophysectomized Rats. Burton L. Baker, John F. Kent, and Edward C. Pliske. *Radiation Res.* 9: 48-58, July 1958. (University of Michigan Medical School, Ann Arbor, Mich.)

An earlier investigation by the authors of the capacity of hypophysectomized rats to survive total-body x-irradiation revealed that 0 to 70 per cent levels of survival are obtained at doses which average about 157 r lower for hypophysectomized than nonhypophysectomized rats (*Proc. Soc. Exper. Biol. & Med.* 89: 142, 1955). This and other studies have also shown that hypophysectomized, irradiated rats exhibit a greater tendency to die early during the gastrointestinal phase of the radiation syndrome than do nonhypophysectomized, irradiated rats.

Further experiments have been carried out in an attempt to answer the following questions: (1) Does hypophysectomy cause structural changes in the small intestine which might account for the increased sensitivity to radiation? (2) Is radiation damage intensified as a consequence of hypophysectomy? (3) Is recovery

from damage induced by x-radiation retarded in the absence of the hypophysis?

Young adult, female Sprague-Dawley rats, weighing 150-185 gm., were divided into four groups: (1) hypophysectomized, nonirradiated; (2) hypophysectomized, irradiated; (3) nonhypophysectomized, nonirradiated; and (4) nonhypophysectomized, irradiated. At varying periods of time (twenty to forty-three days) after hypophysectomy whole-body x-radiation was administered, 500 r, 600 r, 775 r, or 1,200 r.

Thirty to eighty-one days after hypophysectomy alone, there was a reduction in the thickness of the duodenal mucosa accompanied by reduction in size of villi and crypts of Lieberkuhn. The epithelial cells associated with these structures were somewhat smaller and in the crypts exhibited a moderate reduction in intensity of cytoplasmic basophilia. Paneth cells were smaller and contained fewer serous granules and less cytoplasmic ribonucleic acid. With shorter postoperative periods these changes were irregular in appearance and of less magnitude. After allowance was made for the alterations induced by hypophysectomy alone, the histologic changes elicited by irradiation, or the rate of recovery from them, were not significantly different in the hypophysectomized as compared with the nonhypophysectomized rats.

None of the structural changes which occurred in the irradiated, hypophysectomized rats seemed adequate to explain the tendency for these animals to die during the gastrointestinal phase of the radiation syndrome. The authors conclude that the explanation for this observation must rest on metabolic or physiologic alterations not demonstrated by the techniques employed in the present experiments. It is suggested that alterations occurring outside of the digestive tract may be involved in bringing about early death, at least in some animals.

Fourteen photomicrographs; 2 tables.

Effect of X-Ray Dose on the Protective Action and Persistence of Rat Bone Marrow in Irradiated, Penicillin-Treated Mice. George W. Santos, Leonard J. Cole, and Patricia L. Roan. *Am. J. Physiol.* 194: 23-27, July 1958. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

Rat bone-marrow cell suspensions injected together with penicillin into mice a few hours following exposure to a low lethal (LD 20) dose of x-rays (600-680 r) elicited no deleterious effect on percentage of survivors at thirty days, or on mean survival times, when compared to irradiated controls treated with penicillin only. Following LD 70-LD 100 x-rays (720-770 r), the injection of rat bone marrow plus penicillin resulted in marked increases in per cent survival at thirty days, as well as later survival. Thus, at 770 r (LD 100), 40 per cent of the treated mice were still alive at one hundred and fifty days. The single injection of penicillin (3.840 U/mouse) together with rat marrow following 870 r exposure significantly decreased the thirty-day mortality, as compared to irradiated mice receiving rat bone marrow alone. In general, rat granulocytes in the peripheral blood, as determined by the alkaline phosphatase histochemical technic, persisted longer at the higher doses of radiation. The data indicate that LAF₁ mice exposed to x-rays in the midlethal dose range are able to "recognize" and dispose of injected foreign rat cells within a few weeks without suffering an enhanced mortality.

One graph; 3 tables.

AUTHORS' ABSTRACT

Effect of Bone Marrow-Spleen Injection After Fast Neutron Irradiation in Mice. Leonard J. Cole and Marie E. Ellis. *Am. J. Physiol.* **194**: 16-22, July 1958. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

Following exposure to midlethal and supralethal doses of 2-Mev and 8-Mev neutrons from the cyclotron, mice were given a single intravenous injection of fresh isologous bone-marrow suspension containing 1×10^6 nucleated cells, or a single intraperitoneal injection of isologous infant spleen homogenate. At neutron doses (550-700 rep), which elicited 100 per cent mortality by eight days in the controls, injection of bone marrow had no beneficial effect on survival. Following neutron doses in the midlethal range (380-400 rep), bone marrow injection elicited a slight increase (relative to buffer-injected controls) in the percentage of survivors at eight days—57 per cent *versus* 35 per cent. During the nine to fourteen-day period, a smaller proportion of mice (as a percentage of eight-day survivors) died in the bone marrow-treated group, compared with the controls—18 per cent *versus* 60 per cent, respectively. The overall thirty-day survival was 23 per cent for the marrow treated, and 14 per cent for the controls. At this dose level, furthermore, deaths occurred during the third and fourth weeks postirradiation in the face of apparently adequate bone-marrow regeneration, as judged histologically, and the time distribution of deaths was essentially the same whether marrow was administered or not. These data, in sharp contrast with those observed following lethal doses of x-rays in mice, imply that the deaths following 2 Mev neutrons in the midlethal range involve a mechanism different from that of x-rays at comparable doses—possibly the consequences of a delayed or secondary intestinal injury.

Four figures; 1 table. **AUTHORS' ABSTRACT**

Effect on Circulating Blood Volume of Partial Shielding of Rat Intestine During X-Irradiation. Marguerite N. Swift and S. Tom Taketa. *Radiation Res.* **8**: 516-525, June 1958. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

A lethal acute intestinal radiation syndrome (death in three to five days) was produced in rats by 1,000 r of x-irradiation. All animals were exposed with head and thoracic regions lead-shielded in order to minimize hematopoietic damage. With the P^{32} -tagged red cell dilution method, circulating blood volume changes were studied in groups of animals that had been exposed with or without additional lead-shielding of a very short segment of ileum, a procedure which decreases intestinal radiation mortality significantly (*e.g.*, from 94 per cent to 18 per cent). Total circulating blood volume decreased markedly in both groups after irradiation, but the loss was significantly less severe ($p < 0.01$) in rats exposed with the ileal segment shielded. Four days after irradiation, blood volumes averaged 63 and 78 per cent of normal in control irradiated and ileal segment-shielded groups, respectively. Although both groups sustained some loss of red cells (*ca.* 10 per cent), the total blood volume losses measured were mainly due to loss of plasma, presumably reflecting fluid loss by way of the intestinal lumen. Plasma volumes averaged 40 and 66 per cent of normal on the fourth day in control and ileal segment-shielded groups, respectively. Rats surviving the critical period for intestinal radiation deaths showed blood volumes approaching normal levels on the sixth day. With the hematocrit

taken as an approximate index of plasma volume change serial determinations made on individual animals of both groups revealed that mortality and survival time were closely related to the degree and rate of plasma loss.

Two graphs; 1 table.

AUTHORS' SUMMARY

The Deposition of the Rare Earths in Bone. J. Jowsey, R. E. Rowland, and J. H. Marshall. *Radiation Res.* **8**: 490-501, June 1958. (Radiological Physics Division, Argonne National Laboratory, Lemont, Ill.)

An earlier investigation showed yttrium, the product of Sr^{90} decay, to be deposited in areas of bone resorption and not in the osteoid matrix (*J. Nuclear Energy* **2**: 168, 1956). This work has been repeated and the observations extended to two other rare earths, cerium and thulium. Yttrium behaves chemically and metabolically in a way similar to cerium and thulium and may be classified with these two elements in the lanthanon rare earth series. Cerium and thulium lie, respectively, at the beginning and near the end of this series.

The investigation may be divided into three parts: (1) The first part is concerned with the *in vivo* histological localization of the three elements in bone tissue by autoradiography and microradiography. (2) The second part consists in separating bone into two components, the organic and inorganic, and in discovering to which fraction the elements are fixed *in vivo*. (3) The third part consists of *in vitro* experiments in which whole bone, bone mineral, organic matrix, and other materials were incubated in media containing one of the three elements.

The first part of the investigation demonstrated that, after intraperitoneal injection, the three isotopes are taken up in the skeleton and appear on nongrowing bone surfaces that microradiographs show to be highly calcified. They are never found in the uncalcified osteoid tissue on growing surfaces.

Rare earths deposited *in vivo* are not removed with the organic fraction during ethylenediamine (ED) treatment but remain with the inorganic fraction. This indicates that the deposition of the isotopes on highly calcified bone surfaces seen in the autoradiographs is associated with the bone mineral and not with any organic constituent.

The third part of the experiment suggests that the substance responsible for the deposition *in vivo* is responsible for uptake *in vitro*. Bone mineral will take up these rare earth elements from plasma *in vitro*; organic material from bone will not.

The results from the three experiments are consistent with one conclusion—the three rare earth isotopes investigated are taken up by bone mineral and are localized on the available resorbing and inactive surfaces of bone tissue.

Three figures; 1 table.

Bone Density Studies With a Gamma Gage. J. Gershon-Cohen, Norman H. Cherry, and Manfred Boehnke. *Radiation Res.* **8**: 509-515, June 1958. (Albert Einstein Medical Center, Philadelphia, Penna.)

In studies of nutrition, a reliable means of determining quantitatively *in vivo* the amount of calcium salts present in human bone is desirable. A gamma-gage technic has been successfully employed for this pur-

pose. The gauge used by the authors has Ir¹⁹² as the source of the gamma-radiation. A protective lead sphere with a collimating aperture is provided for housing. Detection of the emerging beam which passes through the tissues under investigation is done with a high-efficiency scintillation counter, also provided with a collimating aperture. The signal from the scintillation counter is cabled to an electronic presentation system. Recording of the thickness \times density is made on a strip chart recorder. Changes in calibration and sensitivity of the strip chart can be made precisely and continuously from a front panel control with the chart adjusted to any one of six speeds.

A measure of the quality of a system for determining density changes in a material can be given by the sensitivity of the system. This is defined as the ratio, expressed in per cent, of the change in density observable to the total density measured. With highly improved technics, the x-ray system can be made to have a sensitivity of approximately 1 per cent. The gamma-gauge system can routinely be made to have a sensitivity of 1 per cent, and with time constants of the order of 100 seconds it can be made to have a sensitivity of 0.1 per cent.

The procedure is described. The authors believe that measurements with the gamma gauge more accurately mirror the density of bones than the impression

gained from mere inspection of roentgenograms. This type of gauge, with its great sensitivity, should be applicable to many other tissue density problems in human subjects.

Five figures, including 3 roentgenograms; 1 table.

Removal of Radioactive Contamination from the Human Skin. Willi C. Born. Strahlentherapie 106: 435-445, July 1958. (In German) (Universitäts-Hautklinik Freiburg i. Br., Germany)

The presence of radioactive substance on the intact skin may be hazardous (*a*) because of its local action; (*b*) because of the possibility of absorption percutaneously, or through inhalation of gas or dust, or perorally (hand to mouth); (*c*) finally through uncontrolled dissemination or spread to other persons. Present methods of removal of radioactive contaminants from the human skin are not completely satisfactory. The author recommends what he designates "adhesive-decontamination." The first strip of adhesive removes about 90 per cent of the radioactivity of the skin. The advantages of a mechanical washing apparatus are also discussed.

The procedure is uncomplicated and is not accompanied by any undesirable reactions.

Nine figures; 4 tables. HERBERT POLLACK, M.D., Chicago, Ill.

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